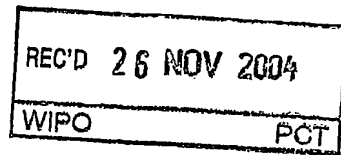




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Patentanmeldung Nr. Patent application No. Demande de brevet n°

04001895.4

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Composition of protein complexes of the app-processing pathway

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**1: FIELD OF THE INVENTION**

The present invention relates to protein complexes of the beta-amyloid precursor protein (APP) processing pathway, component proteins of the said complexes, fragments and derivatives of the component proteins, and antibodies specific to the complexes. The present invention also relates to methods for use of the complexes of the APP processing pathway and their interacting proteins in, inter alia, screening, diagnosis, and therapy, as well as to methods of preparing the complexes.

**2. BACKGROUND OF THE INVENTION (cited references are listed in supra)**

Alzheimer's disease is a chronic condition that affects millions of individuals worldwide. After onset of the disease sufferers require a high degree of supervision and care. As the proportion of aged individuals in the population increases, the number of sufferers of Alzheimer's disease is expected to expand dramatically. Current top drugs (e.g. Aricept®/donepezil) attempt to achieve a temporary improvement of cognitive functions by inhibiting acetylcholinesterase, which results in increased levels of the neurotransmitter acetylcholine in the brain. These therapies are not suitable for later stages of the disease, they do not treat the underlying disease pathology, and they do not halt disease progression. The growing need for an effective therapy, coupled with the absence of effective treatments, presents a significant opportunity for drug target development and drug discovery.

The brains of sufferers of Alzheimer's disease show a characteristic pathology of prominent neuropathologic lesions, such as the initially intracellular neurofibrillary tangles (NFTs), and the extracellular amyloid-rich senile plaques. These lesions are associated with massive loss of populations of CNS neurons and their progression accompanies the clinical dementia associated with AD. The major component of amyloid plaques is the amyloid beta peptide. Amyloid beta is the proteolytic product of a precursor protein, beta amyloid precursor protein (beta-APP or APP). APP is a type-I trans-membrane protein which is cleaved by several different membrane-associated proteases. The first cleavage of APP occurs extracellularly by one of two proteases, alpha-secretase or beta-secretase. Beta-secretase or BACE1 (beta-site APP-cleaving enzyme) is a type-I transmembrane protein containing an aspartyl protease activity (described in detail below). Alpha secretase is a metalloprotease whose activity is most likely to be provided

by one or a combination of the proteins ADAM10 and ADAM17. Following either the beta or alpha cleavage of APP, the final cleavage event occurs within the membrane and is carried out by a protein complex called gamma secretase. It is the combination of the beta and gamma secretase activities that results in the liberation of the Abeta peptides of 40 and 42 residues (there are also lower levels of other forms) from the APP and ultimately the formation of the amyloid plaques responsible for the pathology of Alzheimer's disease. It is believed that the Abeta-42 peptide is the most critical Abeta species, because it shows the most pronounced neurotoxicity, and can aggregate easily, thus forming a nucleus for the aggregation of other Abeta peptides, such as the Abeta-40 which is typically produced at higher levels than the other species.

The applicant's proprietary proteomics technology (TAP/LC-MS/MS) is particularly successful in the elucidation of membrane protein complexes. These multiprotein complexes form the core of the APP processing pathway and are not amenable to other techniques. Known proteins with an important functional role in APP processing were analysed with The applicant's technology to comprehensively chart the dynamic protein interactions that contribute to Abeta production. Selected novel targets are subsequently validated using cellular or biochemical assays. Moreover, purified multi-protein complexes (e.g. beta- or gamma-secretase) do represent defined functional molecular machines, which are used to evaluate the mechanism of known compounds and for the optimisation of leads.

### **Presenilins**

Presenilins 1 and 2 (PS1 and PS2) are integral membrane proteins which are localised in the endoplasmic reticulum, the Golgi and also at the cell surface (1). They are predominantly found as a heterodimers of the NTF and CTF endoproteolytic fragments. The protease that cleaves presenilins (the "presenilinase") is not known, it is likely that the process is autocatalytic, also the functional significance of PS (auto)proteolysis is unclear.

Presenilins are involved in the proteolytical processing of Amyloid precursor protein (APP) (2,3) and the Notch receptor (4,5). In addition, Presenilins are associated with the cell-adhesion proteins alpha and beta-catenin, N-cadherin, and E-cadherin (6) (7) and other members of the armadillo family (8) (9) (10) (11).

APP processing by Presenilins is through their effects on gamma-secretase which cleaves APP, generating the C-terminus of the A-beta peptide. PS1 associates with the C83 and C99 processed C-terminal fragments of APP (12), Nicastrin (13) and Pen-2 (14). Aph-1 (15) (14) is required in Presenilin processing. It is not clear whether Presenilins regulate gamma-secretase activity directly or whether they are protease enzymes themselves (16). The gamma secretase activity could comprise a multimeric complex of these proteins (13) (17) but it is not known how the relationship between these proteins affects secretase activity.

Familial Alzheimer's disease (FAD) patients carry mutations in the presenilin proteins (PS1; PS2) or in APP. These mutations result in increased production of A-beta42 (18) which is the main component of cerebral plaques in FAD (19).

Understanding the composition of the gamma-secretase complex, the relationship between its component parts and its regulation are important in the design of drugs for use in Alzheimer's disease patients.

### **Nicastrin**

Nicastrin is a type 1 trans-membrane glycoprotein with a conserved transmembrane domain and DYIGS motif (13) which is constitutively expressed in neural cell lines (20). Biochemical studies have shown that Nicastrin binds to Presenilins 1 and 2, C-terminal derivatives of APP (13), membrane-tethered forms of Notch (21) and that it is a member of the gamma-secretase complex along with PS1 and PS2 (17). Gamma secretase activity is involved in the cleavage of both Notch and APP. It has been shown that Nicastrin is required for the intra-membrane cleavage of Notch (22) and APP (23), it may also have a role in post-translational stabilisation of Presenilin (24).

Aph-1 (15) and Pen-2 (14) were cloned recently in a screen for presenilin enhancers ("pen") in *C. elegans* and shown to interact genetically with Aph-2 (Nicastrin). Defects in Aph-1 affect Notch signalling and Nicastrin localisation (15). Aph-1 and Pen-2 are required for Notch cleavage, gamma-secretase activity and the accumulation of processed Presenilins. Francis et al. (14) cloned the putative human orthologues of these genes, Aph-1a, Aph-1b and Pen-2, and recently Lee et al. (25) also cloned the human Aph-1 cDNAs.

The exact components of the gamma-secretase complex are not known but these two novel proteins could be components of or accessory factors to the complex and may interact together directly with Presenilin or with a Presenilin/Nicastrin complex. Nicastrin

is therefore a member of the active gamma-secretase complex and there is recent evidence that it is the fully glycosylated form of the protein which is important in this complex. (26-30)

### **Aph-1**

Goutte et al. (15) cloned aph-1 from *C. elegans*. Aph-1 encodes a novel conserved membrane protein with seven hydrophobic regions which are predicted to be membrane spanning. It has a 40 amino acid hydrophilic tail. *C. elegans* aph1 mutants have a phenotype which is indicative of a defect in Notch signalling. In these mutants, Aph-2 (Nicastrin) localisation is altered from being at the cell surface to being in the cytoplasm, concentrated around the nucleus. In *C. elegans*, Aph-1 interacts genetically with Aph-2 (Nicastrin) and Sel-12 (one of the *C. elegans* Presenilin genes) (14).

There are Human, Mouse, *Drosophila* Aph-1 homologues which are potential orthologues. Recently, the human Aph-1 homologues, hAph-1a and hAph-1b have been cloned (14,25). Aph-1a, the hypothetical CGI-78 protein, and Sambiasin (European Patent Application 02014244.4 are all products of the same gene. Francis et al (14) showed that Aph-1 and Pen-2 are required for Notch cleavage, gamma-secretase activity and the accumulation of processed Presenilins in cultured *Drosophila* cells.

Lee et al. (25) cloned two splice variants of Aph-1a called Aph-1aS and Aph-1aL and Aph-1b. They have shown that mammalian Aph-1aL associates with Nicastrin and PS1 NTF/CTF heterodimers and with PS2 and Nicastrin in cultured cells and that endogenous Aph1aL associates with Nicastrin and PS1 in rat brain. Inhibition of the expression of Aph1a reduces the expression of both PS1 and PS2 but not Nicastrin and results in the accumulation of gamma-secretase substrates and the reduction of Aβ. Aph1a was also shown to be required for Notch cleavage.

Aph-1 may have a role in the maturation and trafficking of Nicastrin but it is necessary for gamma-secretase function and may be a member of the gamma-secretase complex.

### **Pen-2**

Francis et al. (14) isolated pen-1 and pen-2 as two presenilin enhancer genes in a genetic screen in *C. elegans*. Pen-1 is identical to Aph-1 (15). Pen-2 has two transmembrane domains and is thought to be a polytopic integral membrane protein. This group cloned the human homologues of Aph-1 and Pen-2. In *C. elegans*, Aph-1 and

Pen-2 interact genetically with Aph-2 (Nicastrin) but not with each other. Hop-1 and Sel-12 are the *C.elegans* presenilin genes. Aph-2 interacts with Hop-1 whereas Aph-1 and Pen-2 interact with Sel-12 (14).

Pen-2 associates with PS1, PS2 and Nicastrin in mammalian cells and Aph-1 and Pen-2 are required for Notch cleavage, gamma-secretase activity and the accumulation of processed Presenilins in cultured *Drosophila* cells (14).

Nicastrin maturation is affected by the levels of PS1 and Pen-2. Loss of PS1 or a reduction in expression of Nicastrin reduces Pen-2 protein levels and a reduction in expression of Pen-2 decreases levels of both PS1, PS2 proteins. In addition, reducing the expression of Pen-2 by RNAi reduces the level of the PS1 complex (31). These data suggest that Pen-2 is either a component of or regulates the assembly of the PS1 complex and that the expression of these proteins is co-ordinately regulated.

### **BACE1 (beta-secretase)**

Vassar et al. (32) cloned a transmembrane aspartic protease that had the characteristics of the postulated beta-secretase of APP. Three other groups also cloned BACE1 using different approaches. BACE1 knockout mice have a normal phenotype, suggesting that therapeutic inhibition of BACE1 for AD may be free of mechanism-based toxicity. BACE1 <sup>-/-</sup> mice who are also homozygous for an amyloid precursor protein transgene lack brain beta-amyloid and beta-secretase-cleaved APP C-terminal fragments. (33). Brain and primary cortical cultures from BACE1 knockout mice showed no detectable beta-secretase activity, and primary cortical cultures from BACE knockout mice produced much less amyloid-beta from APP. This suggests that BACE1, rather than its paralogue BACE2, is the main beta-secretase for APP.

BACE1 is a protein of 501 amino acids containing a 21-aa signal peptide followed by a proprotein domain spanning aa 22 to 45. There are alternatively spliced forms, BACE-I-457 and BACE-I-476. The luminal domain of the mature protein is followed by one predicted transmembrane domain and a short cytosolic C-terminal tail of 24 aa. BACE1 is predicted to be a type 1 transmembrane protein with the active site on the luminal side of the membrane, where beta-secretase cleaves APP and possible other yet unidentified substrates. BACE1 mRNA in rat brain is present at higher levels in neurons than in glia, supporting that neurons are the primary source of the extracellular A-beta deposited in plaques. Sequence and mass spectrometry analyses showed that asn153, asn172, asn223, and asn354 of the BACE1 ectodomain are N-glycosylation

sites. In addition, the ectodomain contains 6 cys residues that form disulfide bridges between positions 216 and 420, 278 and 443, and 330 and 380. The C-terminal domain of BACE1 contains a dileucine motif (LL499/500) that can potentially regulate its trafficking and endocytosis, and an adjacent serine, which is a casein kinase 1 phosphorylation site (S498) (34). The propeptide is predominantly cleaved from BACE1 by furin (35). In cells expressing wt or Swedish mutant APP, transient overexpression of BACE1 decreased alpha-secretase cleavage and increased beta-secretase activity at the known beta-secretase positions, asp1 and glu11. Although BACE1 is clearly a key enzyme required for the processing of APP into Ab, other potential substrates and functions of BACE1 are unknown. Also, no BACE1 interacting proteins with regulatory or modulatory functions have been described. Proteins that activate BACE1 activity would form suitable intervention points for Alzheimer's disease therapy. In addition, proteins that inhibit BACE1, like substrates or pseudosubstrates, could also provide suitable means of intervention e.g. as proteins therapeutics.

#### **APP and the beta-CTF ("C99")**

APP is the precursor of Abeta, a peptide which forms the principal component of Alzheimer disease (AD) senile plaques (3) Masters et al. purified the cerebral amyloid protein that forms the plaque core in AD and Down syndrome. Van Nostrand et al. (36) presented evidence that nexin-II, a protease inhibitor that is synthesized and secreted by extravascular cells, is identical to APP. Multhaup et al. (37) demonstrated that APP is involved in copper reduction. They postulated that copper-mediated toxicity may contribute to neurodegeneration in AD, possibly by increased production of hydroxyl radicals. Yan et al. (38) reported that the receptor for advanced glycation end products RAGE is a receptor for the a-beta peptide and that expression of this receptor increases in AD. Expression of RAGE is particularly increased in neurons close to deposits of amyloid beta peptide and to neurofibrillary tangles. Kaneko et al. (39) demonstrated that nanomolar concentrations of various synthetic beta amyloids specifically impaired mitochondrial succinate dehydrogenase, and speculated that one of the primary targets of beta amyloids is the mitochondrial electron transport chain.

Several missense mutations in the APP gene have been identified that result in early-onset AD: the Swedish APP670/671 double mutation; 3 different mutations at codon 717: the London APP717 mutation, V717I, V717F, and V717G; and the Florida APP716 mutation (Reviewed by Bertram and Tanzi (40)). Most of these AD-related

mutations involve amino acid changes near the beta- and gamma-secretase cleavage sites. Two other missense mutations in the APP gene are located within A-beta near the alpha-secretase cleavage site: the Flemish APP692 mutation, which is associated with cerebral hemorrhage due to congophilic amyloid angiopathy or with early-onset AD with onset age in the mid-forties; and the Dutch APP693 mutation. Almost all AD-linked mutations do elevate secretion of A-beta-42, however, APP693 does not. (41)

Cao and Sudhof (42) demonstrated that the cytoplasmic tail of APP forms a complex with the nuclear adaptor protein Fe65 and the histone acetyltransferase TIP60. This complex stimulates transcription via heterologous Gal4 or LexA DNA binding domains, suggesting that release of the cytoplasmic tail of APP by gamma-cleavage may function in gene expression. The complex could modify expression of genes that function in inflammation (43) or apoptosis (44).

Weggen et al. (45) reported that the nonsteroidal antiinflammatory drugs ibuprofen, indomethacin, and sulindac can decrease the levels of high amyloidogenic amyloid-beta-42 peptide produced from a variety of cultured cells by as much as 80%. This effect was not seen in all NSAIDs and seemed not to be mediated by inhibition of cyclooxygenase (Cox) activity. Weggen et al. (2001) also demonstrated that short-term administration of ibuprofen to mice that produce APP lowered their brain levels of amyloid-beta-42. In cultured cells, the decrease in amyloid-beta-42 secretion was accompanied by an increase in the amyloid-beta(1-38) isoform, indicating that NSAIDs subtly alter gamma-secretase activity without significantly perturbing other APP processing pathways or Notch cleavage.

Proteins and other factors that regulate APP processing, and especially those that influence levels of Abeta-42 versus other Abeta species, form important potential targets in AD therapy.

### **Calsenilin**

In a yeast two-hybrid screen with the C-terminus of Presenilin 2, a neuronal EF-hand (calcium-binding) protein was identified and named "calsenilin" (46). It interacted with both Presenilin 1 and Presenilin 2 in cells and regulated the levels of a proteolytic product of Presenilin 2. Calsenilin is identical to KChIP3, a protein which was found in a yeast two-hybrid screen for proteins interacting with A-type potassium channels (Kv4.3) (47). KChIP3 i) increased the density of Kv4.2 currents indicating a stabilisation of the

channels at the plasma membrane; ii) shifted the current to hyperpolarized potentials; iii) slowed down the kinetics of inactivation and increased the kinetics of recovery.

Calsenilin is also identical to the transcriptional repressor DREAM which acts constitutively to suppress prodynorphin expression in spinal cord neurons (48). Knocking out DREAM results in sufficient dynorphin expression to produce a strong reduction in generalized pain behavior, highlighting the role that intracellular molecules play in modulating pain gating in the spinal cord. Hence proteins that modulate Calsenilin/DREAM activity are interesting targets in nociception.

### Tau

Neurofibrillary tangles (NFT), intraneuronal tau protein deposits, are hallmarks of several neurodegenerative disorders such as Alzheimer's and Pick's disease, frontotemporal dementia, cortico-basal degeneration and progressive supranuclear palsy.

The seven tau isoforms are all products of a single gene. Alternative splicing gives rise to six mRNA species differentially expressed in the CNS, depending on stage of neuronal maturation and neuron type. Tau is found mainly in the axon whereas a related protein, MAP2, is mainly found in dendrites.

Tau and MAP2 are microtubule-associated proteins (MAPs) which coassemble with microtubules and colocalise with microtubules in cells. Tau is a nonstructured molecule with a microtubule binding site containing 3 or 4 characteristic amino acid repeat in its carboxyl-terminal half. Alonso et al. (49) noted that in the brains of AD patients the neuronal cytoskeleton is progressively disrupted and replaced by tangles of paired helical filaments (PHFs), and that PHFs are composed mainly of hyperphosphorylated forms of tau. They demonstrated that in solution normal tau associated with the hyperphosphorylated AD P-tau to form large tangles of filaments. They also demonstrated that dephosphorylation with alkaline phosphatase abolished the ability of AD P-tau to aggregate in vitro. In a form of autosomal dominant inherited dementia known as FTDP17 or Pick disease, the tau gene carries missense mutations or mutations in the 5'- splice site of exon 10, which results in increased levels of tau isoforms with 4 microtubule-binding repeats. These mutations lead to tau molecules that show reduced affinity for microtubules or are more prone to self aggregation.

Proteins and other factors that influence the affinity of tau protein for microtubules, and moreover, influence the aggregation of tau, which is probably mediated by



phosphorylation and dephosphorylation events, are important potential targets in AD therapy.

### **Fe65**

Fe65 is a PTB domain- and WW domain-containing adaptor protein that is part of protein complexes at the plasma membrane as well as in the nucleus: It interacts with the Alzheimer's disease amyloid precursor protein (APP; (50)) and related proteins APLP1 and APLP2 (51). Binding of Fe65 to the cytoplasmic tail of APP enhances production of amyloid-forming Abeta peptides (52), but the molecular mechanism of this amyloidogenic effect of Fe65 has not been elucidated. Furthermore, Fe65 stabilizes APP intracellular domain (AICD) (APP intracellular domain (AICD)), the cytosolic product of APP cleavage by gamma-secretase, (53) and forms a nuclear protein complex with TIP60 (42). Little is known about the functional consequences of Fe65-dependent transactivation. The important role of TIP60 in interleukin-1beta- and NF-KappaB-dependent transactivation (43) suggests, however, that the Fe65 complex might function in inflammation.

Fe65 has been shown to bind to the transcription factor CP2/LSF/LBP1 (54) and the low-density lipoprotein receptor-related protein (55), but the significance of these interactions is unknown. Finally, Fe65 has been observed to block cell cycle progression by downregulating thymidylate synthase expression via an unknown mechanism (56).

Understanding the composition of the Fe65 complex, the relationship between its component parts and its regulation might therefore be important in the design of drugs for use in Alzheimer's disease patients as well as for the treatment of various inflammatory conditions and cancer.

### **X11beta**

X11beta/Mint-2 is a neuronal adaptor protein that is believed to be involved in signal transduction processes. It is also regarded as a putative vesicular trafficking protein in the brain that can form a complex with the potential to couple synaptic vesicle exocytosis to neuronal cell adhesion (57).

X11beta interacts with the Alzheimer's disease amyloid precursor protein (APP) (50). Acting synergistically with Munc18a (58), X11beta stabilises APP and inhibits production of proteolytic APP fragments including the A beta peptide that is deposited in the brains of Alzheimer's disease patients (59).

Via a mechanism that depends on its PDZ domain (yet has otherwise not been characterized), X11beta potently inhibits transactivation by an APP-Gal4/VP16 fusion protein (58). Besides interacting with APP, X11beta binds to the C-terminus of presenilin1, although not as strongly as does X11alpha (58). In addition, X11beta has been reported to interact with XB51 (60), but the functional significance of this interaction is unknown.

In *Drosophila*, dX11beta overexpression in eye imaginal disks causes disruption of compound eye morphology due to enhanced apoptosis of neuronal cells (61). X11beta has been shown to bind to NF-KappaB-p65 through its PDZ domain. This interaction has been implicated in NF-KappaB-dependent Abeta 1-42 production (62).

Elucidation of X11beta complex composition and regulation might therefore help develop novel ways of therapeutic intervention in Alzheimer's disease and inflammation.

### **3. SUMMARY OF THE INVENTION**

An object of the present invention was to identify protein complexes of the beta-amyloid precursor protein (APP) processing pathway, component proteins of the said complexes, fragments and derivatives of the component proteins, and antibodies specific to the complexes. The present invention also relates to methods for use of the protein complexes of the APP processing pathway and their interacting proteins in, inter alia, screening, diagnosis, and therapy, as well as to methods of preparing the complexes.

By applying the process according to the invention said complexes were identified. The components are listed in table 1.

Said object is further achieved by the characterization of component proteins. These proteins are listed in table 2.

Thus, the invention relates to the following embodiments:

1. A protein complex selected from complex (I) and comprising
  - (a) at least one first protein, which first protein is selected from the group of proteins in table 1, fourth column of a given complex, or a functionally active derivative

thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of said protein, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid encoding said protein under low stringency conditions; and

(b) at least one second protein, which second protein is selected from the group of proteins in table 1, fifth column of said given complex, or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of said second protein, said variant being encoded by a nucleic acid that hybridizes to the nucleic acid encoding said protein under low stringency conditions; and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4) 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.

2. A protein complex comprising a first protein selected from the proteins listed in table 1, fourth column of a given complex or a homologue or variant thereof, or a functionally active fragment or functionally active derivative of said first protein, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid of said first protein under low stringency conditions, and at least one second protein selected from the group of proteins in table 1, fifth column of a given complex, or a variant or homologue thereof, or a functionally active fragment or a functionally active derivative of said second protein, the variant of said second protein being encoded by a nucleic acid that hybridizes to the nucleic acid of said second protein under low-stringency conditions, and wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4) 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.

3. A protein complex comprising all proteins selected from the proteins in table 1, third column of a given complex or at least one protein being a homologue thereof, or a variant thereof or functionally active fragment or functionally active derivative of said protein, said variant being encoded by a nucleic acid that hybridizes to the nucleic acid of said protein under low stringency conditions;  
wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.
4. A protein complex that comprises all proteins as listed in table 1, third column for a given complex or at least one protein being a homologue or a variant thereof, or a functionally active fragment or a functionally active derivative thereof, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid of any of said proteins under low stringency conditions, except at least one protein of the proteins listed in table 5, third column, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C, with the proviso that the complex comprises at least one protein selected from table 1, fifth column of a given complex.
5. The complex of any of No. 1 - 4 comprising at least one functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein.

6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.
7. The complex of any of No. 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.
8. The complex of any of No. 1 - 7 that is involved in at least one biochemical activity as stated in table 3.
9. A process for preparing a complex of any of No. 1 - 8 and optionally the components thereof comprising the following steps:  
expressing a protein of the complex, preferably a tagged protein, in a target cell, or a tissue or an organ, isolating the protein complex which is attached to the protein, preferably the tagged protein, and optionally disassociating the protein complex and isolating the individual complex members.
10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.
11. The process according to any of No. 9 - 10 wherein the two tags are separated by a cleavage site for a protease.
12. Component of a protein complex obtainable by a process according to any of No. 9 - 11.
13. Protein selected from the group of proteins in table 1, sixth column of a given complex or a homologue or a variant of thereof, or a functionally active fragment or a functionally active derivative of said protein, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid encoding said protein under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X

SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.

14. Nucleic acid encoding a protein according to No. 13.
15. Construct, preferably a vector construct, comprising
  - (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or
  - (b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative thereof, or a homologue or a variant thereof, at least one of said proteins being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, being selected from the second group of proteins according to No. 1 (b) or
  - (c) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative thereof, or a homologue or a variant thereof, said proteins being selected from the proteins of complex (II) according to No. 1.
16. Host cell, containing a vector comprising at least one nucleic acid of No. 14 and /or a construct of No. 15 or containing several vectors each comprising at least one nucleic acid encoding at least one protein selected from the first group of proteins according to No. 1 (a) and at least one nucleic acid encoding at least one protein selected from the second group of proteins according to No. 1 (b).
17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody containing the binding domain thereof which binds to any of the proteins of the group of proteins according to No. 13.
18. A kit comprising in one or more containers:
  - (a) the complex of any of No. 1 - 8 and/or the proteins of No. 13 and/or
  - (b) an antibody according to No. 17 and/or

- (c) a nucleic acid encoding a protein of the complex of any of No. 1 – 8 and/or a protein of No. 13 and/or
- (d) cells expressing the complex of any of No. 1 – 8 and/or a protein of No. 13 and, optionally,
- (e) further components such as reagents, buffers and working instructions.

19. The kit according to No. 18 for processing a substrate of a complex of any one of No. 1 - 8.

20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as those as stated in column 2, table 4 of a given complex.

21. Array, preferably a microarray, in which at least a complex according to any of No. 1 - 8 and/or at least one protein according to No. 13 and/or at least one antibody according to No. 17 is attached to a solid carrier.

22. A process for modifying a substrate of a complex of any one of No. 1 - 8 comprising the step of bringing into contact a complex of any of No. 1 - 8 with said substrate; such that said substrate is modified.

23. A pharmaceutical composition comprising the protein complex of any of No. 1 - 8 and/or a protein according to No. 13.

24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders, preferentially for diseases or disorders such as those as stated in column 2, table 4 of a given complex.

25. A method for screening for a molecule that binds to a complex of any one of No. 1 - 8 and/or a protein of No. 13, comprising the following steps:  
(a) exposing said complex or protein, or a cell or organism containing said complex or said protein, to one or more candidate molecules; and  
(b) determining whether said candidate molecule is bound to the complex or protein.

26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of a complex of any one of No. 1 - 8 comprising the steps of:

- (a) exposing said complex, or a cell or organism containing said complex to one or more candidate molecules; and
- (b) determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene regulated by the complex and/or the abundance and/or activity of a protein or protein complex dependent upon the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene regulated by the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity, or composition of said complex.

27. The method of No. 26, wherein the amount of said complex is determined.

28. The method of No. 26, wherein the activity of said complex is determined.

29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.

30. The method of No. 26, wherein the amount of the individual protein components of said complex is determined.



31. The method of No. 30, wherein said determining step comprises determining whether any of the proteins listed in table 1, third column of said complex, or a functionally active fragment or a functionally active derivative thereof, or a variant or a homologue thereof, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid of said protein under low-stringency conditions, is present in the complex.
32. The method of any of No. 26 - 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder, preferentially of a disease or disorder selected from the diseases or disorders such as those as stated in column 2, table 4 of a given complex.
33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 - 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder, preferentially of a disease or disorder such as those as stated in column 2, table 4 of a given complex.
34. A method for the production of a pharmaceutical composition comprising carrying out the method of No. 26 - 31 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.
35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, component disposition of, or intracellular localization of the complex of any one of the No. 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene regulated by the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in a corresponding sample from a subject not having the disease or disorder or predisposition indicated the presence in the subject of the disease or disorder or predisposition in the subject.

36. The method of No. 35, wherein the amount of said complex is determined.
37. The method of No. 35, wherein the activity of said complex is determined.
38. The method of No. 37, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.
39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.
40. The method of No. 39, wherein said determining step comprises determining whether any of the proteins according to No. 13 is present in the complex.
41. The complex of any one of No. 1 - 8, or a protein of No. 13 or an antibody or fragment thereof of No. 17, for use in a method of diagnosing a disease or disorder, preferentially of a disease or disorder such as neurodegenerative disease such as those as stated in column 2, table 4 of a given complex.
42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity of, component composition of or intracellular localization of, the complex of any one of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, activity of, or protein composition of, said complex.
43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.

44. The method according to No. 42, wherein said disease or disorder involves increased levels of the amount or activity of said complex.
45. Complex of No. 1 - 8 and/or a protein as listed in table 1, fifth column of said complex as a target for an active agent of a pharmaceutical, preferably a drug target, in the treatment or prevention of a disease or disorder, preferentially of a disease or disorder such as a neurodegenerative disease such as those as stated in column 2, table 4 of a given complex.

### 3.1 DEFINITIONS

The term "activity" as used herein, refers to the function of a molecule in its broadest sense. It generally includes, but is not limited to, biological, biochemical, physical or chemical functions of the molecule. It includes for example the enzymatic activity, the ability to interact with other molecules and ability to activate, facilitate, stabilize, inhibit, suppress or destabilize the function of other molecules, stability, ability to localize to certain subcellular locations. Where applicable, said term also relates to the function of a protein complex in its broadest sense.

The term "agonist" as used herein, means a molecule which modulates the formation of a protein complex or which, when bound to a complex or protein of the invention or a molecule in the protein complex, increases the amount of, or prolongs the duration of, the activity of the complex. The stimulation may be direct or indirect, including effects on the expression of a gene encoding a member of the protein complex, or by a competitive or non-competitive mechanism. Agonists may include proteins, nucleic acids, carbohydrates or any other organic or inorganic molecule or metals. Agonists also include a functional peptide or peptide fragment derived from a protein member of the complexes of the invention or a protein member itself of the complexes of the invention. Preferred activators are those which, when added to the complex and/or the protein of the invention under physiological conditions and/or in vitro assays, including diagnostic or prognostic assays, result in a change of the level of any of the activities of the protein complex and/or the proteins of the invention as exemplary illustrated above by at least 10%, at least 25%, at least 50%, at least 100%, at least, 200%, at least 500% or at least 1000% at a concentration of the activator  $1\mu\text{g ml}^{-1}$ ,  $10\mu\text{g ml}^{-1}$ ,  $100\mu\text{g ml}^{-1}$ ,  $500\mu\text{g ml}^{-1}$ ,  $1\text{mg ml}^{-1}$ ,  $10\text{mg ml}^{-1}$  or  $100\text{mg ml}^{-1}$ . Any combination of the

above mentioned degrees of percentages and concentration may be used to define an agonist of the invention, with greater effect at lower concentrations being preferred.

The term "amount" as used herein and as applicable to the embodiment described relates to the amount of the particular protein or protein complex described, including the value of null, i.e. where no protein or protein complex described in that particular embodiment is present under the or any of the conditions which might be specified in that particular embodiment.

The term "animal" as used herein includes, but is not limited to mammals, preferably mammals such as cows, pigs, horses, mice, rats, cats, dogs, sheep, goats and most preferably humans. Other animals used in agriculture, such as chickens, ducks etc. are also included in the definition as used herein.

The term "animal" as used herein does not include humans if being used in the context of genetic alterations to the germline.

The term "antagonist" as used herein, means a molecule which modulates the formation of a protein complex or which, when bound to a complex or protein of the invention or a molecule in the protein complex, decreases the amount of, or the duration or level of activity of the complex. The effect may be direct or indirect, including effects on the expression of a gene encoding a member of the protein complex, or by a competitive or non-competitive mechanism. Antagonists may include proteins, including antibodies, nucleic acids, carbohydrates or any other organic or inorganic molecule or metals. Antagonists also include a functional peptide or peptide fragment derived from a protein member of the complexes of the invention or a protein member itself of the complexes of the invention. Preferred antagonists are those which, when added to the complex and/or the protein of the invention under physiological conditions and/or in vitro assays, including diagnostic or prognostic assays, result in a change of the level of any of the activities of the protein complex and/or the proteins of the invention as exemplarily illustrated above by at least 10%, at least 20%, at least 30%, at least 40% at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, at least 95% or at least 99% at a concentration of the inhibitor of  $1\mu\text{g ml}^{-1}$ ,  $10\mu\text{g ml}^{-1}$ ,  $100\mu\text{g ml}^{-1}$ ,  $500\mu\text{g ml}^{-1}$ ,  $1\text{mg ml}^{-1}$ ,  $10\text{mg ml}^{-1}$  or  $100\text{mg ml}^{-1}$ .

Any combination of the above mentioned degrees of percentages and concentration may be used to define antagonist of the invention, with greater effect at lower concentrations being preferred.

The term "antibodies" as used herein, include include, but are not limited to, polyclonal, monoclonal, chimeric, single chain, Fab fragments, and an Fab expression library.

The term "binding" as used herein means a stable or transient association between two molecules, including electrostatic, hydrophobic, ionic and/or hydrogen-bond interaction under physiological conditions and/or conditions being used in diagnostic or prognostic method or process or procedure.

The term "carrier" as used herein refers to a diluent, adjuvant, excipient, or vehicle with which the therapeutic is administered. Such pharmaceutical carriers can be sterile liquids, such as water and oils, including those of petroleum, animal, vegetable or synthetic origin, including but not limited to peanut oil, soybean oil, mineral oil, sesame oil and the like. Water is a preferred carrier when the pharmaceutical composition is administered orally. Saline and aqueous dextrose are preferred carriers when the pharmaceutical composition is administered intravenously. Saline solutions and aqueous dextrose and glycerol solutions are preferably employed as liquid carriers for injectable solutions. Suitable pharmaceutical excipients include starch, glucose, lactose, sucrose, gelatin, malt, rice, flour, chalk, silica gel, sodium stearate, glycerol monostearate, talc, sodium chloride, dried skim milk, glycerol, propylene, glycol, water, ethanol and the like. The composition, if desired, can also contain minor amounts of wetting or emulsifying agents, or pH buffering agents. These compositions can take the form of solutions, suspensions, emulsions, tablets, pills, capsules, powders, sustained-release formulations and the like. The composition can be formulated as a suppository, with traditional binders and carriers such as triglycerides. Oral formulation can include standard carriers such as pharmaceutical grades of mannitol, lactose, starch, magnesium stearate, sodium saccharine, cellulose, magnesium carbonate, etc. Examples of suitable pharmaceutical carriers are described in "Remington's Pharmaceutical Sciences" by E.W. Martin. Such compositions will contain a therapeutically effective amount of the therapeutic, preferably in purified form, together with a suitable amount of carrier so as to provide the form for proper administration to the patient. The formulation should suit the mode of administration.

If not stated otherwise, the terms "complex" and "protein complex" are used interchangeably herein and refer to a complex of proteins that is able to perform one or more functions of the wild type protein complex. The protein complex may or may not include and/or be associated with other molecules such as nucleic acid, such as RNA or

DNA, or lipids or further cofactors or moieties selected from a metal ions, hormones, second messengers, phosphate, sugars.

A "complex" of the invention may also be part of or a unit of a larger physiological protein assembly.

The term "component of the APP processing pathway" as used herein refers to a protein and/or protein complex which is involved in mediating APP processing in a cell. Components of the APP processing pathway include the following protein complexes as provided herein and components thereof:

Aph1a-complex, APP-695SW-complex, APP-C99-complex, Fe65-complex, Nicastrin-complex, Psen-2-complex, Pen2-complex, Tau-complex, X11 $\beta$ -complex

If not stated otherwise, the term "compound" as used herein are include but are not limited to peptides, nucleic acids, carbohydrates, natural product extract libraries, organic molecules, preferentially small organic molecules, anorganic molecules, including but not limited to chemicals, metals and organometallic molecules.

The terms "derivatives" or "analogs of component proteins" or "variants" as used herein include, but are not limited, to molecules comprising regions that are substantially homologous to the component proteins, in various embodiments, by at least 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95% or 99% identity over an amino acid sequence of identical size or when compared to an aligned sequence in which the alignment is done by a computer homology program known in the art, or whose encoding nucleic acid is capable of hybridizing to a sequence encoding the component protein under stringent, moderately stringent, or nonstringent conditions. It means a protein which is the outcome of a modification of the naturally occurring protein, by amino acid substitutions, deletions and additions, respectively, which derivatives still exhibit the biological function of the naturally occurring protein although not necessarily to the same degree. The biological function of such proteins can e.g. be examined by suitable available in vitro assays as provided in the invention.

The term "functionally active" as used herein refers to a polypeptide, namely a fragment or derivative, having structural, regulatory, or biochemical functions of the protein according to the embodiment of which this polypeptide, namely fragment or derivative is related to.

The term "fragment" as used herein refers to a polypeptide of at least 10, 20, 30, 40 or 50 amino acids of the component protein according to the embodiment. In specific embodiments, such fragments are not larger than 35, 100 or 200 amino acids.

The term "gene" as used herein refers to a nucleic acid comprising an open reading frame encoding a polypeptide of, if not stated otherwise, the present invention, including both exon and optionally intron sequences.

The terms "homologue" or "homologous gene products" as used herein mean a protein in another species, preferably mammals, which performs the same biological function as the a protein component of the complex further described herein. Such homologues are also termed "orthologous gene products". The algorithm for the detection of orthologue gene pairs from humans and mammalians or other species uses the whole genome of these organisms. First, pairwise best hits are retrieved, using a full Smith-Waterman alignment of predicted proteins. To further improve reliability, these pairs are clustered with pairwise best hits involving *Drosophila melanogaster* and *C. elegans* proteins. Such analysis is given, e.g., in Nature, 2001, 409:860-921. The homologues of the proteins according to the invention can either be isolated based on the sequence homology of the genes encoding the proteins provided herein to the genes of other species by cloning the respective gene applying conventional technology and expressing the protein from such gene, or by isolating proteins of the other species by isolating the analogous complex according to the methods provided herein or to other suitable methods commonly known in the art.

The term "host cells" or, were applicable, "cells" or "hosts" as used herein is intended to be understood in a broadest sense and include, but are not limited to mammalian cell systems infected with virus (e.g., vaccinia virus, adenovirus, etc.); insect cell systems infected with virus (e.g., baculovirus); microorganisms such as yeast containing yeast vectors; or bacteria transformed with bacteriophage, DNA, plasmid DNA, or cosmid DNA. The expression elements of vectors vary in their strengths and specificities. Depending on the host-vector system utilized, any one of a number of suitable transcription and translation elements may be used. It is understood that this term not only refers to the particular subject cell but to the progeny or potential progeny of such a cell. Because certain modifications may occur in succeeding generations due to either mutation of environmental influences, such progeny may not, in fact, be identical to the parent cell, but are still included within the scope of the term as used herein.

The term "modification" as used herein refers to all modifications of a protein or protein complex of the invention including cleavage and addition or removal of a group.

The term "nucleic acid" as used herein refers to polynucleotides such as deoxyribonucleic acid (DNA), and, where appropriate, ribonucleic acid (RNA). They may

also be polynucleotides which include within them synthetic or modified nucleotides. A number of different types of modification to polynucleotides are known in the art. These include methylphosphonate and phosphorothioate backbones, addition of acridine or polylysine chains at the 3' and/or 5' ends of the molecule. For the purposes of the present invention, it is to be understood that the polynucleotides described herein may be modified by any method available in the art. Such modifications may be carried out in order to enhance the in vivo activity or lifespan of polynucleotides of the invention. Polynucleotides according to the invention may be produced recombinantly, synthetically, or by any means available to those of skill in the art. They may also be cloned by standard techniques. The polynucleotides are typically provided in isolated and/or purified form. As applicable to the embodiment being described, they include both single stranded and double-stranded polynucleotides.

The term "percent identity", as used herein, means the number of identical residues as defined by an optimal alignment using the Smith-Waterman algorithm divided by the length of the overlap multiplied by 100. The alignment is performed by the search program (Pearson, 1991, Genomics 11:635-650) with the constraint to align the maximum of both sequences.

The terms "polypeptides" and "proteins" are, where applicable, used interchangeably herein. They may be chemically modified, e.g. post-translationally modified. For example, they may be glycosylated or comprise modified amino acid residues. They may also be modified by the addition of a signal sequence to promote their secretion from a cell where the polypeptide does not naturally contain such a sequence. They may be tagged with a tag. They may be tagged with different labels which may assist in identification of the proteins in a protein complex. Polypeptides/proteins for use in the invention may be in a substantially isolated form. It will be understood that the polypeptid/protein may be mixed with carriers or diluents which will not interfere with the intended purpose of the polypeptide and still be regarded as substantially isolated. A polypeptide/protein for use in the invention may also be in a substantially purified form, in which case it will generally comprise the polypeptide in a preparation in which more than 50%, e.g. more than 80%, 90%, 95% or 99%, by weight of the polypeptide in the preparation is a polypeptide of the invention.

"Target for therapeutic drug" means that the respective protein (target) can bind the active ingredient of a pharmaceutical composition and thereby changes its biological activity in response to the drug binding.



The term "tag" as used herein is meant to be understood in its broadest sense and to include, but is not limited to any suitable enzymatic, fluorescent, or radioactive labels and suitable epitopes, including but not limited to HA-tag, Myc-tag, T7, His-tag, FLAG-tag, Calmodulin binding proteins, glutathione-S-transferase, strep-tag, KT3-epitope, EEF-epitopes, green-fluorescent protein and variants thereof.

The term "therapeutics" as used herein, includes, but is not limited to, a protein complex of the present invention, the individual component proteins, and analogs and derivatives (including fragments); antibodies thereto; nucleic acids encoding the component protein, and analogs or derivatives thereof; component protein antisense nucleic acids, and agents that modulate complex formation and/or activity (i.e., agonists and antagonists).

The term "vector" as used herein means a nucleic acid molecule capable of transporting another nucleic acid sequence to which it has been linked. Preferred vectors are those capable of autonomous replication and/or expression of nucleic acids to which they linked. The terms "plasmid" and "vector" are used interchangeably herein when applicable to the embodiment. However, vectors other than plasmids are also included herein. The expression elements of vectors vary in their strengths and specificities. Depending on the host-vector system utilized, any one of a number of suitable transcription and translation elements may be used.

#### **4. DETAILED DESCRIPTION OF THE INVENTION**

##### **Overview:**

An object of the present invention was to identify protein complexes of the beta-amyloid precursor protein (APP) processing pathway, component proteins of the said complexes, fragments and derivatives of the component proteins, and antibodies specific to the complexes. The present invention also relates to methods for use of the protein complexes of the APP processing pathway and their interacting proteins in, inter alia, screening, diagnosis, and therapy, as well as to methods of preparing the complexes.

By applying the process according to the invention said protein complex were identified. The components are listed in table 1.

Said object is further achieved by the characterisation of component proteins. These proteins are listed in table 2.

The invention thus relates to the following embodiments:

1. A protein complex selected from complex (I) and comprising
  - (a) at least one first protein, which first protein is selected from the group of proteins in table 1, fourth column of a given complex, or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of said protein, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid encoding said protein under low stringency conditions; and
  - (b) at least one second protein, which second protein is selected from the group of proteins in table 1, fifth column of said given complex, or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of said second protein, said variant being encoded by a nucleic acid that hybridizes to the nucleic acid encoding said protein under low stringency conditions; and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4) 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.
2. A protein complex comprising a first protein selected from the proteins listed in table 1, fourth column of a given complex or a homologue or variant thereof, or a functionally active fragment or functionally active derivative of said first protein, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid of said first protein under low stringency conditions, and at least one second protein selected from the group of proteins in table 1, fifth column of a given complex, or a variant or homologue thereof, or a functionally active fragment or a functionally active derivative of said second protein, the variant of said second protein being encoded by a nucleic acid that hybridizes to the nucleic acid of said second protein under low-

stringency conditions, and wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4) 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.

3. A protein complex comprising all proteins selected from the proteins in table 1, third column of a given complex or at least one protein being a homologue thereof, or a variant thereof or functionally active fragment or functionally active derivative of said protein, said variant being encoded by a nucleic acid that hybridizes to the nucleic acid of said protein under low stringency conditions;  
wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.
4. A protein complex that comprises all proteins as listed in table 1, third column for a given complex or at least one protein being a homologue or a variant thereof, or a functionally active fragment or a functionally active derivative thereof, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid of any of said proteins under low stringency conditions, except at least one protein of the proteins listed in table 5, third column, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C, with the proviso that the

complex comprises at least one protein selected from table 1, fifth column of a given complex.

5. The complex of any of No. 1 - 4 comprising at least one functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein.
6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.
7. The complex of any of No. 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.
8. The complex of any of No. 1 - 7 that is involved in at least one biochemical activity as stated in table 3.
9. A process for preparing a complex of any of No. 1 - 8 and optionally the components thereof comprising the following steps:  
expressing a protein of the complex, preferably a tagged protein, in a target cell, or a tissue or an organ, isolating the protein complex which is attached to the protein, preferably the tagged protein, and optionally disassociating the protein complex and isolating the individual complex members.
10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.
11. The process according to any of No. 9 - 10 wherein the two tags are separated by a cleavage site for a protease.
12. Component of a protein complex obtainable by a process according to any of No. 9 - 11.

13. Protein selected from the group of proteins in table 1, sixth column of a given complex or a homologue or a variant of thereof, or a functionally active fragment or a functionally active derivative of said protein, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid encoding said protein under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.
14. Nucleic acid encoding a protein according to No. 13.
15. Construct, preferably a vector construct, comprising
- (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or
  - (b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative thereof, or a homologue or a variant thereof, at least one of said proteins being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, being selected from the second group of proteins according to No. 1 (b) or
  - (c) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative thereof, or a homologue or a variant thereof, said proteins being selected from the proteins of complex (II) according to No. 1.
16. Host cell, containing a vector comprising at least one nucleic acid of No. 14 and /or a construct of No. 15 or containing several vectors each comprising at least one nucleic acid encoding at least one protein selected from the first group of proteins according to No. 1 (a) and at least one nucleic acid encoding at least one protein selected from the second group of proteins according to No. 1 (b).

17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody containing the binding domain thereof which binds to any of the proteins of the group of proteins according to No. 13.
18. A kit comprising in one or more containers:
- (a) the complex of any of No. 1 – 8 and/or the proteins of No. 13 and/or
  - (b) an antibody according to No. 17 and/or
  - (c) a nucleic acid encoding a protein of the complex of any of No. 1 – 8 and/or a protein of No. 13 and/or
  - (d) cells expressing the complex of any of No. 1 – 8 and/or a protein of No. 13 and, optionally,
  - (e) further components such as reagents, buffers and working instructions.
19. The kit according to No. 18 for processing a substrate of a complex of any one of No. 1 - 8.
20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as those as stated in column 2, table 4 of a given complex.
21. Array, preferably a microarray, in which at least a complex according to any of No. 1 - 8 and/or at least one protein according to No. 13 and/or at least one antibody according to No. 17 is attached to a solid carrier.
22. A process for modifying a substrate of a complex of any one of No. 1 - 8 comprising the step of bringing into contact a complex of any of No. 1 - 8 with said substrate, such that said substrate is modified.
23. A pharmaceutical composition comprising the protein complex of any of No. 1 - 8 and/or a protein according to No. 13.

24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders, preferentially for diseases or disorders such as those as stated in column 2, table 4 of a given complex.
25. A method for screening for a molecule that binds to a complex of any one of No. 1 - 8 and/or a protein of No. 13, comprising the following steps:
- (a) exposing said complex or protein, or a cell or organism containing said complex or said protein, to one or more candidate molecules; and
  - (b) determining whether said candidate molecule is bound to the complex or protein.
26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of a complex of any one of No. 1 - 8 comprising the steps of:
- (a) exposing said complex, or a cell or organism containing said complex to one or more candidate molecules; and
  - (b) determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene regulated by the complex and/or the abundance and/or activity of a protein or protein complex dependent upon the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene regulated by the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity, or composition of said complex.
27. The method of No. 26, wherein the amount of said complex is determined.
28. The method of No. 26, wherein the activity of said complex is determined.

29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.
30. The method of No. 26, wherein the amount of the individual protein components of said complex is determined.
31. The method of No. 30, wherein said determining step comprises determining whether any of the proteins listed in table 1, third column of said complex, or a functionally active fragment or a functionally active derivative thereof, or a variant or a homologue thereof, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid of said protein under low-stringency conditions, is present in the complex.
32. The method of any of No. 26 - 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder, preferentially of a disease or disorder selected from the diseases or disorders such as those as stated in column 2, table 4 of a given complex.
33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 - 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder, preferentially of a disease or disorder such as those as stated in column 2, table 4 of a given complex.
34. A method for the production of a pharmaceutical composition comprising carrying out the method of No. 26 - 31 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.
35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or



disorder is characterized by an aberrant amount of, component disposition of, or intracellular localization of the complex of any one of the No. 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene regulated by the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in a corresponding sample from a subject not having the disease or disorder or predisposition indicated the presence in the subject of the disease or disorder or predisposition in the subject.

36. The method of No. 35, wherein the amount of said complex is determined.

37. The method of No. 35, wherein the activity of said complex is determined.

38. The method of No. 37, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.

39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.

40. The method of No. 39, wherein said determining step comprises determining whether any of the proteins according to No. 13 is present in the complex.

41. The complex of any one of No. 1 - 8, or a protein of No. 13 or an antibody or fragment thereof of No. 17, for use in a method of diagnosing a disease or disorder, preferentially of a disease or disorder such as neurodegenerative disease such as those as stated in column 2, table 4 of a given complex.

42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity of, component composition of or intracellular localization of, the complex of any one of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, activity of, or protein composition of, said complex.
43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.
44. The method according to No. 42, wherein said disease or disorder involves increased levels of the amount or activity of said complex.
45. Complex of No. 1 - 8 and/or a protein as listed in table 1, fifth column of said complex as a target for an active agent of a pharmaceutical, preferably a drug target, in the treatment or prevention of a disease or disorder, preferentially of a disease or disorder such as a neurodegenerative disease such as those as stated in column 2, table 4 of a given complex.

Animal models are also provided herein.

Preferably, the protein components of the complexes described herein are all mammalian proteins. The complexes can also consist only of the respective homologues from other mammals such as mouse, rat, pig, cow, dog, monkey, sheep or horse or other species such as *D. melanogaster*, *C. elegans* or chicken. In another preferred embodiment, the complexes are a mixture of proteins from two or more species.

#### TABLES:

##### Table 1: Composition of Complexes

First column ('Name of complex'): Lists the name of the protein complexes as used herein.

Second column ('Entry point'): Lists the bait proteins that have been chosen for the purification of the given complex.

Third column ('All interactors'): Lists all novel interactors which have been identified as members of the complex and all interactors which have been known to be associated with the bait so far.

Fourth column ('Known interactors'): Lists all interactors which have been known to be associated with the bait so far.

Fifth column ('Novel interactors of the complex'): Lists all novel interactors of the complex which have been identified in the experiments provided herein.

Sixth column: Separately lists the members of the newly identified complex which have not been annotated previously.

#### Table 2: Individual Proteins of the Complexes

First column ('Protein'): Lists in alphabetical order all proteins which have been identified as interactors of the complexes presented herein.

Second column ('SEQ ID'): Lists the SEQ ID (Sequence Identifications) of the proteins herein as used herein.

Third column ('IPI-Numbers'): Lists the IPI-Numbers of the proteins herein. The IPI-Numbers refer to the International Protein Index created by the European Bioinformatics Institute (EMBL-EBI), Hinxton, UK.

Fourth column ('Molecular Weight'): Lists the Molecular Weight of the proteins in Dalton.

#### Table 3: Biochemical Activities of the Complexes of the invention.

First column ('Name of complex'): Lists the name of the protein complexes as used herein.

Second column ('Biochemical Activity'): Lists biochemical activities of the complexes. Assays in order to test these activities are also provided herein (infra).

#### Table 4: Medical Applications of the Complexes of the invention

First column ('Name of complex'): Lists the name of the protein complexes as used herein

Second column ('Medical application'): lists disorder, diseases, disease areas etc. which are treatable and/or preventable and/or diagnosable etc. by therapeutics and methods interacting with/acting via the complex.

### 4.1 PROTEIN COMPLEXES/PROTEINS OF THE INVENTION

The protein complexes of the present invention and their component proteins are described in the Tables 1 - 4. The protein complexes and component proteins can be obtained by methods well known in the art for protein purification and recombinant protein expression. For example, the protein complexes of the present invention can be isolated using the TAP method described in Section 5, *infra*, and in WO 00/09716 and Rigaut et al., 1999, *Nature Biotechnol.* 17:1030-1032, which are each incorporated by reference in their entirety. Additionally, the protein complexes can be isolated by immunoprecipitation of the component proteins and combining the immunoprecipitated proteins. The protein complexes can also be produced by recombinantly expressing the component proteins and combining the expressed proteins.

The nucleic and amino acid sequences of the component proteins of the protein complexes of the present invention are provided herein (SEQ.ID NO 1 - 315), and can be obtained by any method known in the art, e.g., by PCR amplification using synthetic primers hybridizable to the 3' and 5' ends of each sequence, and/or by cloning from a cDNA or genomic library using an oligonucleotide specific for each nucleotide sequence.

Homologues (e.g., nucleic acids encoding component proteins from other species) or other related sequences (e.g., variants, paralogs) which are members of a native cellular protein complex can be obtained by low, moderate or high stringency hybridization with all or a portion of the particular nucleic acid sequence as a probe, using methods well known in the art for nucleic acid hybridization and cloning.

Exemplary moderately stringent hybridization conditions are as follows: prehybridization of filters containing DNA is carried out for 8 hours to overnight at 65°C in buffer composed of 6X SSC, 50 mM Tris-HCl (pH 7.5), 1 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.02% BSA, and 500 µg/ml denatured salmon sperm DNA. Filters are hybridized for 48 hours at 65°C in prehybridization mixture containing 100 µg/ml denatured salmon sperm DNA and 5-20 X 10<sup>6</sup> cpm of <sup>32</sup>P-labeled probe. Washing of filters is done at 37°C for 1 hour in a solution containing 2X SSC, 0.01% PVP, 0.01% Ficoll, and 0.01% BSA. This is followed by a wash in 0.1X SSC at 50 °C for 45 min before autoradiography. Alternatively, exemplary conditions of high stringency are as follows: e.g., hybridization to filter-bound DNA in 0.5 M NaHPO<sub>4</sub>, 7% sodium dodecyl sulfate (SDS), 1 mM EDTA at 65°C, and washing in 0.1xSSC/0.1% SDS at 68°C (Ausubel et al., eds., 1989, *Current Protocols in Molecular Biology*, Vol. 1, Green Publishing Associates, Inc., and John Wiley & sons, Inc., New York, at p. 2.10.3). Other conditions of high stringency which may be

used are well known in the art. Exemplary low stringency hybridization conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100  $\mu$ g/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.

For recombinant expression of one or more of the proteins, the nucleic acid containing all or a portion of the nucleotide sequence encoding the protein can be inserted into an appropriate expression vector, i.e., a vector that contains the necessary elements for the transcription and translation of the inserted protein coding sequence. The necessary transcriptional and translational signals can also be supplied by the native promoter of the component protein gene, and/or flanking regions.

A variety of host-vector systems may be utilized to express the protein coding sequence. These include but are not limited to mammalian cell systems infected with virus (e.g., vaccinia virus, adenovirus, etc.); insect cell systems infected with virus (e.g., baculovirus); microorganisms such as yeast containing yeast vectors; or bacteria transformed with bacteriophage, DNA, plasmid DNA, or cosmid DNA. The expression elements of vectors vary in their strengths and specificities. Depending on the host-vector system utilized, any one of a number of suitable transcription and translation elements may be used.

In a preferred embodiment, a complex of the present invention is obtained by expressing the entire coding sequences of the component proteins in the same cell, either under the control of the same promoter or separate promoters. In yet another embodiment, a derivative, fragment or homologue of a component protein is recombinantly expressed. Preferably the derivative, fragment or homologue of the protein forms a complex with the other components of the complex, and more preferably forms a complex that binds to an anti-complex antibody. Such an antibody is further described infra.

Any method available in the art can be used for the insertion of DNA fragments into a vector to construct expression vectors containing a chimeric gene consisting of appropriate transcriptional/translational control signals and protein coding sequences. These methods may include in vitro recombinant DNA and synthetic techniques and in vivo recombinant techniques (genetic recombination). Expression of nucleic acid

sequences encoding a component protein, or a derivative, fragment or homologue thereof, may be regulated by a second nucleic acid sequence so that the gene or fragment thereof is expressed in a host transformed with the recombinant DNA molecule(s). For example, expression of the proteins may be controlled by any promoter/enhancer known in the art. In a specific embodiment, the promoter is not native to the gene for the component protein. Promoters that may be used can be selected from among the many known in the art, and are chosen so as to be operative in the selected host cell.

In a specific embodiment, a vector is used that comprises a promoter operably linked to nucleic acid sequences encoding a component protein, or a fragment, derivative or homologue thereof, one or more origins of replication, and optionally, one or more selectable markers (e.g., an antibiotic resistance gene).

In another specific embodiment, an expression vector containing the coding sequence, or a portion thereof, of a component protein, either together or separately, is made by subcloning the gene sequences into the EcoRI restriction site of each of the three pGEX vectors (glutathione S-transferase expression vectors; Smith and Johnson, 1988, Gene 7:31-40). This allows for the expression of products in the correct reading frame.

Expression vectors containing the sequences of interest can be identified by three general approaches: (a) nucleic acid hybridization, (b) presence or absence of "marker" gene function, and (c) expression of the inserted sequences. In the first approach, coding sequences can be detected by nucleic acid hybridization to probes comprising sequences homologous and complementary to the inserted sequences. In the second approach, the recombinant vector/host system can be identified and selected based upon the presence or absence of certain "marker" functions (e.g., resistance to antibiotics, occlusion body formation in baculovirus, etc.) caused by insertion of the sequences of interest in the vector. For example, if a component protein gene, or portion thereof, is inserted within the marker gene sequence of the vector, recombinants containing the encoded protein or portion will be identified by the absence of the marker gene function (e.g., loss of  $\beta$ -galactosidase activity). In the third approach, recombinant expression vectors can be identified by assaying for the component protein expressed by the recombinant vector. Such assays can be based, for example, on the physical or functional properties of the interacting species in in vitro assay systems, e.g., formation of a complex comprising the protein or binding to an anti-complex antibody.

Once recombinant component protein molecules are identified and the complexes or individual proteins isolated, several methods known in the art can be used to propagate them. Using a suitable host system and growth conditions, recombinant expression vectors can be propagated and amplified in quantity. As previously described, the expression vectors or derivatives which can be used include, but are not limited to, human or animal viruses such as vaccinia virus or adenovirus; insect viruses such as baculovirus, yeast vectors; bacteriophage vectors such as lambda phage; and plasmid and cosmid vectors.

In addition, a host cell strain may be chosen that modulates the expression of the inserted sequences, or modifies or processes the expressed proteins in the specific fashion desired. Expression from certain promoters can be elevated in the presence of certain inducers; thus expression of the genetically-engineered component proteins may be controlled. Furthermore, different host cells have characteristic and specific mechanisms for the translational and post-translational processing and modification (e.g., glycosylation, phosphorylation, etc.) of proteins. Appropriate cell lines or host systems can be chosen to ensure that the desired modification and processing of the foreign protein is achieved. For example, expression in a bacterial system can be used to produce an unglycosylated core protein, while expression in mammalian cells ensures "native" glycosylation of a heterologous protein. Furthermore, different vector/host expression systems may effect processing reactions to different extents.

In other specific embodiments, a component protein or a fragment, homologue or derivative thereof, may be expressed as fusion or chimeric protein product comprising the protein, fragment, homologue, or derivative joined via a peptide bond to a heterologous protein sequence of a different protein. Such chimeric products can be made by ligating the appropriate nucleic acid sequences encoding the desired amino acids to each other by methods known in the art, in the proper coding frame, and expressing the chimeric products in a suitable host by methods commonly known in the art. Alternatively, such a chimeric product can be made by protein synthetic techniques, e.g., by use of a peptide synthesizer. Chimeric genes comprising a portion of a component protein fused to any heterologous protein-encoding sequences may be constructed.

In particular, protein component derivatives can be made by altering their sequences by substitutions, additions or deletions that provide for functionally equivalent molecules. Due to the degeneracy of nucleotide coding sequences, other DNA

sequences that encode substantially the same amino acid sequence as a component gene or cDNA can be used in the practice of the present invention. These include but are not limited to nucleotide sequences comprising all or portions of the component protein gene that are altered by the substitution of different codons that encode a functionally equivalent amino acid residue within the sequence, thus producing a silent change. Likewise, the derivatives of the invention include, but are not limited to, those containing, as a primary amino acid sequence, all or part of the amino acid sequence of a component protein, including altered sequences in which functionally equivalent amino acid residues are substituted for residues within the sequence resulting in a silent change. For example, one or more amino acid residues within the sequence can be substituted by another amino acid of a similar polarity that acts as a functional equivalent, resulting in a silent alteration. Substitutes for an amino acid within the sequence may be selected from other members of the class to which the amino acid belongs. For example, the nonpolar (hydrophobic) amino acids include alanine, leucine, isoleucine, valine, proline, phenylalanine, tryptophan and methionine. The polar neutral amino acids include glycine, serine, threonine, cysteine, tyrosine, asparagine, and glutamine. The positively charged (basic) amino acids include arginine, lysine and histidine. The negatively charged (acidic) amino acids include aspartic acid and glutamic acid.

In a specific embodiment, up to 1%, 2%, 5%, 10%, 15% or 20% of the total number of amino acids in the wild type protein are substituted or deleted; or 1, 2, 3, 4, 5, or 6 or up to 10 or up to 20 amino acids are inserted, substituted or deleted relative to the wild type protein.

In a specific embodiment of the invention, the nucleic acids encoding a protein component and protein components consisting of or comprising a fragment of or consisting of at least 6 (continuous) amino acids of the protein are provided. In other embodiments, the fragment consists of at least 10, 20, 30, 40, or 50 amino acids of the component protein. In specific embodiments, such fragments are not larger than 35, 100 or 200 amino acids. Derivatives or analogs of component proteins include, but are not limited, to molecules comprising regions that are substantially homologous to the component proteins, in various embodiments, by at least 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95% or 99% identity over an amino acid sequence of identical size or when compared to an aligned sequence in which the alignment is done by a computer homology program known in the art, or whose encoding nucleic acid is capable of



hybridizing to a sequence encoding the component protein under stringent, moderately stringent, or nonstringent conditions.

In a specific embodiment, proteins are provided herein, which share an identical region of 20, 30, 40, 50 or 60 contiguous amino acids of the proteins listed in table 2.

The protein component derivatives and analogs of the invention can be produced by various methods known in the art. The manipulations which result in their production can occur at the gene or protein level. For example, the cloned gene sequences can be modified by any of numerous strategies known in the art (Sambrook et al., 1989, Molecular Cloning, A Laboratory Manual, 2d Ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York). The sequences can be cleaved at appropriate sites with restriction endonuclease(s), followed by further enzymatic modification if desired, isolated, and ligated in vitro. In the production of the gene encoding a derivative, homologue or analog of a component protein, care should be taken to ensure that the modified gene retains the original translational reading frame, uninterrupted by translational stop signals, in the gene region where the desired activity is encoded.

Additionally, the encoding nucleic acid sequence can be mutated in vitro or in vivo, to create and/or destroy translation, initiation, and/or termination sequences, or to create variations in coding regions and/or form new restriction endonuclease sites or destroy pre-existing ones, to facilitate further in vitro modification. Any technique for mutagenesis known in the art can be used, including but not limited to, chemical mutagenesis and in vitro site-directed mutagenesis (Hutchinson et al., 1978, J. Biol. Chem. 253:6551-6558), amplification with PCR primers containing a mutation, etc.

Once a recombinant cell expressing a component protein, or fragment or derivative thereof, is identified, the individual gene product or complex can be isolated and analyzed. This is achieved by assays based on the physical and/or functional properties of the protein or complex, including, but not limited to, radioactive labeling of the product followed by analysis by gel electrophoresis, immunoassay, cross-linking to marker-labeled product, etc.

The component proteins and complexes may be isolated and purified by standard methods known in the art (either from natural sources or recombinant host cells expressing the complexes or proteins), including but not restricted to column chromatography (e.g., ion exchange, affinity, gel exclusion, reversed-phase high pressure, fast protein liquid, etc.), differential centrifugation, differential solubility, or by

any other standard technique used for the purification of proteins. Functional properties may be evaluated using any suitable assay known in the art.

Alternatively, once a component protein or its derivative, is identified, the amino acid sequence of the protein can be deduced from the nucleic acid sequence of the chimeric gene from which it was encoded. As a result, the protein or its derivative can be synthesized by standard chemical methods known in the art (e.g., Hunkapiller et al., 1984, Nature 310:105-111).

Manipulations of component protein sequences may be made at the protein level. Included within the scope of the invention is a complex in which the component proteins or derivatives and analogs that are differentially modified during or after translation, e.g., by glycosylation, acetylation, phosphorylation, amidation, derivatization by known protecting/blocking groups, proteolytic cleavage, linkage to an antibody molecule or other cellular ligand, etc. Any of numerous chemical modifications may be carried out by known techniques, including but not limited to specific chemical cleavage by cyanogen bromide, trypsin, chymotrypsin, papain, V8 protease, NaBH<sub>4</sub>, acetylation, formylation, oxidation, reduction, metabolic synthesis in the presence of tunicamycin, etc.

In specific embodiments, the amino acid sequences are modified to include a fluorescent label. In another specific embodiment, the protein sequences are modified to have a heterofunctional reagent; such heterofunctional reagents can be used to crosslink the members of the complex.

In addition, complexes of analogs and derivatives of component proteins can be chemically synthesized. For example, a peptide corresponding to a portion of a component protein, which comprises the desired domain or mediates the desired activity in vitro (e.g., complex formation) can be synthesized by use of a peptide synthesizer. Furthermore, if desired, non-classical amino acids or chemical amino acid analogs can be introduced as a substitution or addition into the protein sequence.

In cases where natural products are suspected of being mutant or are isolated from new species, the amino acid sequence of a component protein isolated from the natural source, as well as those expressed in vitro, or from synthesized expression vectors in vivo or in vitro, can be determined from analysis of the DNA sequence, or alternatively, by direct sequencing of the isolated protein. Such analysis can be performed by manual sequencing or through use of an automated amino acid sequenator.

The complexes can also be analyzed by hydrophilicity analysis (Hopp and Woods, 1981, Proc. Natl. Acad. Sci. USA 78:3824-3828). A hydrophilicity profile can be used to identify the hydrophobic and hydrophilic regions of the proteins, and help predict their orientation in designing substrates for experimental manipulation, such as in binding experiments, antibody synthesis, etc. Secondary structural analysis can also be done to identify regions of the component proteins, or their derivatives, that assume specific structures (Chou and Fasman, 1974, Biochemistry 13:222-23). Manipulation, translation, secondary structure prediction, hydrophilicity and hydrophobicity profile predictions, open reading frame prediction and plotting, and determination of sequence homologies, etc., can be accomplished using computer software programs available in the art.

Other methods of structural analysis including but not limited to X-ray crystallography (Engstrom, 1974, Biochem. Exp. Biol. 11:7-13), mass spectroscopy and gas chromatography (Methods in Protein Science, J. Wiley and Sons, New York, 1997), and computer modeling (Fletterick and Zoller, eds., 1986, Computer Graphics and Molecular Modeling, In: Current Communications in Molecular Biology, Cold Spring Harbor Laboratory, Cold Spring Harbor Press, New York) can also be employed.

#### 4.2 ANTIBODIES TO PROTEIN COMPLEXES/PROTEINS OF THE INVENTION

According to the present invention, a protein complex of the present invention comprising a first protein, or a functionally active fragment or functionally active derivative thereof, selected from the group consisting of proteins listed in fourth column of table 1; and a second protein, or a functionally active fragment or functionally active derivative thereof, selected from the group consisting of proteins listed in fifth column of table 1, or a functionally active fragment or functionally active derivative thereof, can be used as an immunogen to generate antibodies which immunospecifically bind such immunogen. According to the present invention, also a protein complex of the present invention can be used as an immunogen to generate antibodies which immunospecifically bind to such immunogen comprising all proteins listed in fifth column of table 1.

Such antibodies include, but are not limited to, polyclonal, monoclonal, chimeric, single chain, Fab fragments, and an Fab expression library. In a specific embodiment, antibodies to a complex comprising human protein components are

produced. In another embodiment, a complex formed from a fragment of said first protein and a fragment of said second protein, which fragments contain the protein domain that interacts with the other member of the complex, are used as an immunogen for antibody production. In a preferred embodiment, the antibody specific for the complex in that the antibody does not bind the individual protein components of the complex.

Polyclonal antibodies can be prepared as described above by immunizing a suitable subject with a polypeptide of the invention as an immunogen. Preferred polyclonal antibody compositions are ones that have been selected for antibodies directed against a polypeptide or polypeptides of the invention. Particularly preferred polyclonal antibody preparations are ones that contain only antibodies directed against a polypeptide or polypeptides of the invention. Particularly preferred immunogen compositions are those that contain no other human proteins such as, for example, immunogen compositions made using a non-human host cell for recombinant expression of a polypeptide of the invention. In such a manner, the only human epitope or epitopes recognized by the resulting antibody compositions raised against this immunogen will be present as part of a polypeptide or polypeptides of the invention.

The antibody titer in the immunized subject can be monitored over time by standard techniques, such as with an enzyme linked immunosorbent assay (ELISA) using immobilized polypeptide. If desired, the antibody molecules can be isolated from the mammal (e.g., from the blood) and further purified by well-known techniques, such as protein A chromatography to obtain the IgG fraction. Alternatively, antibodies specific for a protein or polypeptide of the invention can be selected for (e.g., partially purified) or purified by, e.g., affinity chromatography. For example, a recombinantly expressed and purified (or partially purified) protein of the invention is produced as described herein, and covalently or non-covalently coupled to a solid support such as, for example, a chromatography column. The column can then be used to affinity purify antibodies specific for the proteins of the invention from a sample containing antibodies directed against a large number of different epitopes, thereby generating a substantially purified antibody composition, i.e., one that is substantially free of contaminating antibodies. By a substantially purified antibody composition is meant, in this context, that the antibody sample contains at most only 30% (by dry weight) of contaminating antibodies directed against epitopes other than those on the desired protein or polypeptide of the invention, and preferably at most 20%, yet more preferably at most 10%, and most preferably at

most 5% (by dry weight) of the sample is contaminating antibodies. A purified antibody composition means that at least 99% of the antibodies in the composition are directed against the desired protein or polypeptide of the invention.

At an appropriate time after immunization, e.g., when the specific antibody titers are highest, antibody-producing cells can be obtained from the subject and used to prepare monoclonal antibodies by standard techniques, such as the hybridoma technique originally described by Kohler and Milstein, 1975, *Nature* 256:495-497, the human B cell hybridoma technique (Kozbor et al., 1983, *Immunol. Today* 4:72), the EBV-hybridoma technique (Cole et al., 1985, *Monoclonal Antibodies and Cancer Therapy*, Alan R. Liss, Inc., pp. 77-96) or trioma techniques. The technology for producing hybridomas is well known (see generally *Current Protocols in Immunology* 1994, Coligan et al. (eds.) John Wiley & Sons, Inc., New York, NY). Hybridoma cells producing a monoclonal antibody of the invention are detected by screening the hybridoma culture supernatants for antibodies that bind the polypeptide of interest, e.g., using a standard ELISA assay.

Alternative to preparing monoclonal antibody-secreting hybridomas, a monoclonal antibody directed against a polypeptide of the invention can be identified and isolated by screening a recombinant combinatorial immunoglobulin library (e.g., an antibody phage display library) with the polypeptide of interest. Kits for generating and screening phage display libraries are commercially available (e.g., the Pharmacia Recombinant Phage Antibody System, Catalog No. 27-9400-01; and the Stratagene SurfZAP Phage Display Kit, Catalog No. 240612). Additionally, examples of methods and reagents particularly amenable for use in generating and screening antibody display library can be found in, for example, U.S. Patent No. 5,223,409; PCT Publication No. WO 92/18619; PCT Publication No. WO 91/17271; PCT Publication No. WO 92/20791; PCT Publication No. WO 92/15679; PCT Publication No. WO 93/01288; PCT Publication No. WO 92/01047; PCT Publication No. WO 92/09690; PCT Publication No. WO 90/02809; Fuchs et al., 1991, *Bio/Technology* 9:1370-1372; Hay et al., 1992, *Hum. Antibod. Hybridomas* 3:81-85; Huse et al., 1989, *Science* 246:1275-1281; Griffiths et al., 1993, *EMBO J.* 12:725-734.

Additionally, recombinant antibodies, such as chimeric and humanized monoclonal antibodies, comprising both human and non-human portions, which can be made using standard recombinant DNA techniques, are within the scope of the invention. A chimeric antibody is a molecule in which different portions are derived from different

animal species, such as those having a variable region derived from a murine mAb and a human immunoglobulin constant region. (See, e.g., Cabilly et al., U.S. Patent No. 4,816,567; and Boss et al., U.S. Patent No. 4,816,397, which are incorporated herein by reference in their entirety.) Humanized antibodies are antibody molecules from non-human species having one or more complementarily determining regions (CDRs) from the non-human species and a framework region from a human immunoglobulin molecule. (See, e.g., Queen, U.S. Patent No. 5,585,089, which is incorporated herein by reference in its entirety.) Such chimeric and humanized monoclonal antibodies can be produced by recombinant DNA techniques known in the art, for example using methods described in PCT Publication No. WO 87/02671; European Patent Application 184,187; European Patent Application 171,496; European Patent Application 173,494; PCT Publication No. WO 86/01533; U.S. Patent No. 4,816,567; European Patent Application 125,023; Better et al., 1988, *Science* 240:1041-1043; Liu et al., 1987, *Proc. Natl. Acad. Sci. USA* 84:3439-3443; Liu et al., 1987, *J. Immunol.* 139:3521-3526; Sun et al., 1987, *Proc. Natl. Acad. Sci. USA* 84:214-218; Nishimura et al., 1987, *Canc. Res.* 47:999-1005; Wood et al., 1985, *Nature* 314:446-449; and Shaw et al., 1988, *J. Natl. Cancer Inst.* 80:1553-1559; Morrison, 1985, *Science* 229:1202-1207; Oi et al., 1986, *Bio/Techniques* 4:214; U.S. Patent 5,225,539; Jones et al., 1986, *Nature* 321:552-525; Verhoeyan et al., 1988, *Science* 239:1534; and Beidler et al., 1988, *J. Immunol.* 141:4053-4060.

Completely human antibodies are particularly desirable for therapeutic treatment of human patients. Such antibodies can be produced, for example, using transgenic mice which are incapable of expressing endogenous immunoglobulin heavy and light chains genes, but which can express human heavy and light chain genes. The transgenic mice are immunized in the normal fashion with a selected antigen, e.g., all or a portion of a polypeptide of the invention. Monoclonal antibodies directed against the antigen can be obtained using conventional hybridoma technology. The human immunoglobulin transgenes harbored by the transgenic mice rearrange during B cell differentiation, and subsequently undergo class switching and somatic mutation. Thus, using such a technique, it is possible to produce therapeutically useful IgG, IgA and IgE antibodies. For an overview of this technology for producing human antibodies, see Lonberg and Huszar, 1995, *Int. Rev. Immunol.* 13:65-93). For a detailed discussion of this technology for producing human antibodies and human monoclonal antibodies and protocols for producing such antibodies, see, e.g., U.S. Patent 5,625,126; U.S. Patent 5,633,425; U.S. Patent 5,569,825; U.S. Patent 5,661,016; and U.S. Patent 5,545,806. In

addition, companies such as Abgenix, Inc. (Freemont, CA), can be engaged to provide human antibodies directed against a selected antigen using technology similar to that described above.

Completely human antibodies which recognize a selected epitope can be generated using a technique referred to as "guided selection." In this approach a selected non-human monoclonal antibody, e.g., a murine antibody, is used to guide the selection of a completely human antibody recognizing the same epitope. (Jespers et al., 1994, *Bio/technology* 12:899-903).

Antibody fragments that contain the idiotypes of the complex can be generated by techniques known in the art. For example, such fragments include, but are not limited to, the F(ab')<sub>2</sub> fragment which can be produced by pepsin digestion of the antibody molecule; the Fab' fragment that can be generated by reducing the disulfide bridges of the F(ab')<sub>2</sub> fragment; the Fab fragment that can be generated by treating the antibody molecular with papain and a reducing agent; and Fv fragments.

In the production of antibodies, screening for the desired antibody can be accomplished by techniques known in the art, e.g., ELISA (enzyme-linked immunosorbent assay). To select antibodies specific to a particular domain of the complex, or a derivative thereof, one may assay generated hybridomas for a product that binds to the fragment of the complex, or a derivative thereof, that contains such a domain. For selection of an antibody that specifically binds a complex of the present, or a derivative, or homologue thereof, but which does not specifically bind to the individual proteins of the complex, or a derivative, or homologue thereof, one can select on the basis of positive binding to the complex and a lack of binding to the individual protein components.

Antibodies specific to a domain of the complex, or a derivative, or homologue thereof, are also provided.

The foregoing antibodies can be used in methods known in the art relating to the localization and/or quantification of the complexes of the invention, e.g., for imaging these proteins, measuring levels thereof in appropriate physiological samples (by immunoassay), in diagnostic methods, etc. This hold true also for a derivative, or homologue thereof of a complex.

In another embodiment of the invention (see *infra*), an antibody to a complex or a fragment of such antibodies containing the antibody binding domain, is a therapeutic.

#### **4.3 DIAGNOSTIC, PROGNOSTIC, AND SCREENING USES OF THE PROTEIN COMPLEXES/PROTEINS OF THE INVENTION**

The particular protein complexes and proteins of the present invention may be markers of normal physiological processes, and thus have diagnostic utility. Further, definition of particular groups of patients with elevations or deficiencies of a protein complex of the present invention, or wherein the protein complex has a change in protein component composition, can lead to new nosological classifications of diseases, furthering diagnostic ability.

Examples for diseases or disorders are those as listed in table 4

Detecting levels of protein complexes, or individual component proteins that form the complexes, or detecting levels of the mRNAs encoding the components of the complex, may be used in diagnosis, prognosis, and/or staging to follow the course of a disease state, to follow a therapeutic response, etc.

A protein complex of the present invention and the individual components of the complex and a derivative, analog or subsequence thereof, encoding nucleic acids (and sequences complementary thereto), and anti-complex antibodies and antibodies directed against individual components that can form the complex, are useful in diagnostics. The foregoing molecules can be used in assays, such as immunoassays, to detect, prognose, diagnose, or monitor various conditions, diseases, and disorders characterized by aberrant levels of a complex or aberrant component composition of a complex, or monitor the treatment of such various conditions, diseases, and disorders.

In particular, such an immunoassay is carried out by a method comprising contacting a sample derived from a patient with an anti-complex antibody under conditions such that immunospecific binding can occur, and detecting or measuring the amount of any immunospecific binding by the antibody. In a specific aspect, such binding of antibody, in tissue sections, can be used to detect aberrant complex localization, or aberrant (e.g., high, low or absent) levels of a protein complex or complexes. In a specific embodiment, an antibody to the complex can be used to assay a patient tissue or serum sample for the presence of the complex, where an aberrant level of the complex is an indication of a diseased condition. By "aberrant levels" is meant increased or decreased levels relative to that present, or a standard level



representing that present, in an analogous sample from a portion or fluid of the body, or from a subject not having the disorder.

The immunoassays which can be used include but are not limited to competitive and non-competitive assay systems using techniques such as Western blots, radioimmunoassays, ELISA (enzyme linked immunosorbent assay), "sandwich" immunoassays, immunoprecipitation assays, precipitin reactions, gel diffusion precipitin reactions, immunodiffusion assays, agglutination assays, complement-fixation assays, immunoradiometric assays, fluorescent immunoassays, protein A immunoassays, to name but a few known in the art.

Nucleic acids encoding the components of the protein complex and related nucleic acid sequences and subsequences, including complementary sequences, can be used in hybridization assays. The nucleic acid sequences, or subsequences thereof, comprising about at least 8 nucleotides, can be used as hybridization probes. Hybridization assays can be used to detect, prognose, diagnose, or monitor conditions, disorders, or disease states associated with aberrant levels of the mRNAs encoding the components of a complex as described, supra. In particular, such a hybridization assay is carried out by a method comprising contacting a sample containing nucleic acid with a nucleic acid probe capable of hybridizing to component protein coding DNA or RNA, under conditions such that hybridization can occur, and detecting or measuring any resulting hybridization.

In specific embodiments, diseases and disorders involving or characterized by aberrant levels of a protein complex or aberrant complex composition can be diagnosed, or its suspected presence can be screened for, or a predisposition to develop such disorders can be detected, by determining the component protein composition of the complex, or detecting aberrant levels of a member of the complex or un-complexed component proteins or encoding nucleic acids, or functional activity including, but not restricted to, binding to an interacting partner, or by detecting mutations in component protein RNA, DNA or protein (e.g., mutations such as translocations, truncations, changes in nucleotide or amino acid sequence relative to wild-type that cause increased or decreased expression or activity of a complex, and/or component protein.

Such diseases and disorders include, but are not limited to neurodegenerative disease such as listed in table 4.

By way of example, levels of a protein complex and the individual components of a complex can be detected by immunoassay, levels of component protein RNA or DNA

can be detected by hybridization assays (e.g., Northern blots, dot blots, RNase protection assays), and binding of component proteins to each other (e.g., complex formation) can be measured by binding assays commonly known in the art. Translocations and point mutations in component protein genes can be detected by Southern blotting, RFLP analysis, PCR using primers that preferably generate a fragment spanning at least most of the gene by sequencing of genomic DNA or cDNA obtained from the patient, etc.

Assays well known in the art (e.g., assays described above such as immunoassays, nucleic acid hybridization assays, activity assays, etc.) can be used to determine whether one or more particular protein complexes are present at either increased or decreased levels, or are absent, in samples from patients suffering from a particular disease or disorder, or having a predisposition to develop such a disease or disorder, as compared to the levels in samples from subjects not having such a disease or disorder, or having a predisposition to develop such a disease or disorder. Additionally, these assays can be used to determine whether the ratio of the complex to the un-complexed components of the complex, is increased or decreased in samples from patients suffering from a particular disease or disorder, or having a predisposition to develop such a disease or disorder, as compared to the ratio in samples from subjects not having such a disease or disorder.

In the event that levels of one or more particular protein complexes (i.e., complexes formed from component protein derivatives, homologs, fragments, or analogs) are determined to be increased in patients suffering from a particular disease or disorder, or having a predisposition to develop such a disease or disorder, then the particular disease or disorder, or predisposition for a disease or disorder, can be diagnosed, have prognosis defined for, be screened for, or be monitored by detecting increased levels of the one or more protein complexes, increased levels of the mRNA that encodes one or more members of the one or more particular protein complexes, or by detecting increased complex functional activity.

Accordingly, in a specific embodiment of the present invention, diseases and disorders involving increased levels of one or more protein complexes can be diagnosed, or their suspected presence can be screened for, or a predisposition to develop such disorders can be detected, by detecting increased levels of the one or more protein complexes, the mRNA encoding both members of the complex, or complex functional activity, or by detecting mutations in the component proteins that stabilize or enhance

complex formation, e.g., mutations such as translocations in nucleic acids, truncations in the gene or protein, changes in nucleotide or amino acid sequence relative to wild-type, that stabilize or enhance complex formation.

In the event that levels of one or more particular protein complexes are determined to be decreased in patients suffering from a particular disease or disorder, or having a predisposition to develop such a disease or disorder, then the particular disease or disorder or predisposition for a disease or disorder can be diagnosed, have its prognosis determined, be screened for, or be monitored by detecting decreased levels of the one or more protein complexes, the mRNA that encodes one or more members of the particular one or more protein complexes, or by detecting decreased protein complex functional activity.

Accordingly, in a specific embodiment of the invention, diseases and disorders involving decreased levels of one or more protein complexes can be diagnosed, or their suspected presence can be screened for, or a predisposition to develop such disorders can be detected, by detecting decreased levels of the one or more protein complexes, the mRNA encoding one or more members of the one or more complexes, or complex functional activity, or by detecting mutations in the component proteins that decrease complex formation, e.g., mutations such as translocations in nucleic acids, truncations in the gene or protein, changes in nucleotide or amino acid sequence relative to wild-type, that decrease complex formation.

Accordingly, in a specific embodiment of the invention, diseases and disorders involving aberrant compositions of the complexes can be diagnosed, or their suspected presence can be screened for, or a predisposition to develop such disorders can be detected, by detecting the component proteins of one or more complexes, or the mRNA encoding the members of the one or more complexes.

The use of detection techniques, especially those involving antibodies against a protein complex, provides a method of detecting specific cells that express the complex or component proteins. Using such assays, specific cell types can be defined in which one or more particular protein complexes are expressed, and the presence of the complex or component proteins can be correlated with cell viability, state, health, etc.

Also embodied are methods to detect a protein complex of the present invention in cell culture models that express particular protein complexes or derivatives thereof, for the purpose of characterizing or preparing the complexes for harvest. This embodiment includes cell sorting of prokaryotes such as but not restricted to bacteria (Davey and Kell,

1996, Microbiol. Rev. 60:641-696), primary cultures and tissue specimens from eukaryotes, including mammalian species such as human (Steele et al., 1996, Clin. Obstet. Gynecol 39:801-813), and continuous cell cultures (Orfao and Ruiz-Arguelles, 1996, Clin. Biochem. 29:5-9). Such isolations can be used as methods of diagnosis, described, supra.

In a further specific embodiment, a modulation of the formation process of a complex can be determined.

Such a modulation can either be a change in the typical time course of its formation or a change in the typical steps leading to the formation of the complete complex.

Such changes can for example be detected by analysing and comparing the process of complex formation in untreated wild type cells of a particular type and/or cells showing or having the predisposition to develop a certain disease phenotype and/or cells which have been treated with particular conditions and/or particular agents in a particular situation.

Methods to study such changes in time course are well known in the art and include for example Western-blot analysis of the proteins in the complex isolated at different steps of its formation.

Furthermore an aberrant intracellular localization of the protein complex and/or an aberrant transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or a gene dependent on the complex can serve as a marker for a disease and thus have diagnostic utility for any disease which is caused by an aberrant activity, function, composition or formation of the complex of the invention.

Methods to study the intracellular localization are well known in the art and include, but are not limited to immunofluorescence analysis using antibodies specific for components of the protein. Preferentially, double-stainings including staining of other cellular structures are being used to facilitate the detection of the intracellular localization. Methods to analyse the transcription levels of a gene dependent on the complex are also well known in the art and include Northern blot analysis, quantitative PCR etc. The abundance of proteins dependent on the protein can be analyzed as described supra. Methods to study changes in the activity of proteins dependent on complex depend on the protein. The choice of such methods will be apparent to any person skilled in the art.

#### 4.4 THERAPEUTIC USES OF PROTEIN COMPLEXES/PROTEINS OF THE INVENTION

The present invention is directed to a method for treatment or prevention of various diseases and disorders by administration of a therapeutic compound (termed herein "therapeutic"). Such "therapeutics" include, but are not limited to, a protein complex of the present invention, the individual component proteins, and analogs and derivatives (including fragments) of the foregoing (e.g., as described hereinabove); antibodies thereto (as described hereinabove); nucleic acids encoding the component protein, and analogs or derivatives, thereof (e.g., as described hereinabove); component protein antisense nucleic acids, and agents that modulate complex formation and/or activity (i.e., agonists and antagonists).

The protein complexes as identified herein can be implicated in processes which are implicated in or associated with pathological conditions.

Diseases and disorders which can be treated and/or prevented and/or diagnosed by therapeutics interacting with any of the complexes provided herein are for example those listed in table 4.

These disorders are treated or prevented by administration of a therapeutic that modulates (i.e. inhibits or promotes) protein complex activity or formation or modulates its function or composition. Diseases or disorders associated with aberrant levels of complex activity or formation, or aberrant levels or activity of the component proteins, or aberrant complex composition or a change in the function, may be treated by administration of a therapeutic that modulates complex formation or activity or by the administration of a protein complex.

Therapeutics may also be administered to modulate complex formation or activity or level thereof in a microbial organism such as yeast, fungi such as candida albicans causing an infectious disease in animals or humans.

Diseases and disorders characterized by increased (relative to a subject not suffering from the disease or disorder) complex levels or activity can be treated with therapeutics that antagonize (i.e., reduce or inhibit) complex formation or activity. Therapeutics that can be used include, but are not limited to, the component proteins or an analog, derivative or fragment of the component protein; anti-complex antibodies (e.g., antibodies specific for the protein complex, or a fragment or derivative of the

antibody containing the binding region thereof; nucleic acids encoding the component proteins; antisense nucleic acids complementary to nucleic acids encoding the component proteins; and nucleic acids encoding the component protein that are dysfunctional due to, e.g., a heterologous insertion within the protein coding sequence, that are used to "knockout" endogenous protein function by homologous recombination, see, e.g., Capecchi, 1989, *Science* 244:1288-1292. In one embodiment, a therapeutic is 1, 2 or more antisense nucleic acids which are complementary to 1, 2, or more nucleic acids, respectfully, that encode component proteins of a complex.

In a specific embodiment of the present invention, a nucleic acid containing a portion of a component protein gene in which gene sequences flank (are both 5' and 3' to) a different gene sequence, is used as a component protein antagonist, or to promote component protein inactivation by homologous recombination (see also, Koller and Smithies, 1989, *Proc. Natl. Acad. Sci. USA* 86:8932-8935; Zijlstra et al., 1989, *Nature* 342: 435-438). Additionally, mutants or derivatives of a component protein that has greater affinity for another component protein or the complex than wild type may be administered to compete with wild type protein for binding, thereby reducing the levels of complexes containing the wild type protein. Other therapeutics that inhibit complex function can be identified by use of known convenient in vitro assays, e.g., based on their ability to inhibit complex formation, or as described in Section 4.5, *infra*.

In specific embodiments, therapeutics that antagonize complex formation or activity are administered therapeutically, including prophylactically, (1) in diseases or disorders involving an increased (relative to normal or desired) level of a complex, for example, in patients where complexes are overactive or overexpressed; or (2) in diseases or disorders where an in vitro (or in vivo) assay (see *infra*) indicates the utility of antagonist administration. Increased levels of a complex can be readily detected, e.g., by quantifying protein and/or RNA, by obtaining a patient tissue sample (e.g., from biopsy tissue) and assaying it in vitro for RNA or protein levels, or structure and/or activity of the expressed complex (or the encoding mRNA). Many methods standard in the art can be thus employed including, but not limited to, immunoassays to detect complexes and/or visualize complexes (e.g., Western blot analysis, immunoprecipitation followed by sodium dodecyl sulfate polyacrylamide gel electrophoresis [SDS-PAGE], immunocytochemistry, etc.), and/or hybridization assays to detect concurrent expression of component protein mRNA (e.g., Northern assays, dot blot analysis, in situ hybridization, etc.).

A more specific embodiment of the present invention is directed to a method of reducing complex expression (i.e., expression of the protein components of the complex and/or formation of the complex) by targeting mRNAs that express the protein moieties. RNA therapeutics currently fall within three classes, antisense species, ribozymes, or RNA aptamers (Good et al., 1997, *Gene Therapy* 4:45-54).

Antisense oligonucleotides have been the most widely used. By way of example, but not limitation, antisense oligonucleotide methodology to reduce complex formation is presented below, *infra*. Ribozyme therapy involves the administration, induced expression, etc. of small RNA molecules with enzymatic ability to cleave, bind, or otherwise inactivate specific RNAs, to reduce or eliminate expression of particular proteins (Grassi and Marini, 1996, *Annals of Medicine* 28:499-510; Gibson, 1996, *Cancer and Metastasis Reviews* 15:287-299). RNA aptamers are specific RNA ligand proteins, such as for Tat and Rev RNA (Good et al., 1997, *Gene Therapy* 4:45-54) that can specifically inhibit their translation. Aptamers specific for component proteins can be identified by many methods well known in the art, for example, by affecting the formation of a complex in the protein-protein interaction assay described, *infra*.

In another embodiment, the activity or levels of a component protein are reduced by administration of another component protein, or the encoding nucleic acid, or an antibody that immunospecifically binds to the component protein, or a fragment or a derivative of the antibody containing the binding domain thereof.

In another aspect of the invention, diseases or disorders associated with increased levels of a component protein of the complex may be treated or prevented by administration of a therapeutic that increases complex formation if the complex formation acts to reduce or inactivate the component protein through complex formation. Such diseases or disorders can be treated or prevented by administration of one component member of the complex, administration of antibodies or other molecules that stabilize the complex, etc.

Diseases and disorders associated with underexpression of a complex, or a component protein, are treated or prevented by administration of a therapeutic that promotes (i.e., increases or supplies) complex levels and/or function, or individual component protein function. Examples of such a therapeutic include but are not limited to a complex or a derivative, analog or fragment of the complex that are functionally active (e.g., able to form a complex), un-complexed component proteins and derivatives, analogs, and fragments of un-complexed component proteins, and nucleic acids

encoding the members of a complex or functionally active derivatives or fragments of the members of the complex, e.g., for use in gene therapy. In a specific embodiment, a therapeutic includes derivatives, homologs or fragments of a component protein that increase and/or stabilize complex formation. Examples of other agonists can be identified using in vitro assays or animal models, examples of which are described, *infra*.

In yet other specific embodiments of the present invention, therapeutics that promote complex function are administered therapeutically, including prophylactically, (1) in diseases or disorders involving an absence or decreased (relative to normal or desired) level of a complex, for example, in patients where a complex, or the individual components necessary to form the complex, is lacking, genetically defective, biologically inactive or underactive, or under-expressed; or (2) in diseases or disorders wherein an in vitro or in vivo assay (see, *infra*) indicates the utility of complex agonist administration. The absence or decreased level of a complex, component protein or function can be readily detected, e.g., by obtaining a patient tissue sample (e.g., from biopsy tissue) and assaying it in vitro for RNA or protein levels, structure and/or activity of the expressed complex and/or the concurrent expression of mRNA encoding the two components of the complex. Many methods standard in the art can be thus employed, including but not limited to immunoassays to detect and/or visualize a complex, or the individual components of a complex (e.g., Western blot analysis, immunoprecipitation followed by sodium dodecyl sulfate polyacrylamide gel electrophoresis [SDS-PAGE], immunocytochemistry, etc.) and/or hybridization assays to detect expression of mRNAs encoding the individual protein components of a complex by detecting and/or visualizing component mRNA concurrently or separately using, e.g., Northern assays, dot blot analysis, in situ hybridization, etc.

In specific embodiments, the activity or levels of a component protein are increased by administration of another component protein of the same complex, or a derivative, homolog or analog thereof, a nucleic acid encoding the other component, or an agent that stabilizes or enhances the other component, or a fragment or derivative of such an agent.

Generally, administration of products of species origin or species reactivity (in the case of antibodies) that is the same species as that of the patient is preferred. Thus, in a preferred embodiment, a human complex, or derivative, homolog or analog thereof; nucleic acids encoding the members of the human complex or a derivative, homolog or analog thereof; an antibody to a human complex, or a derivative thereof; or other human



agents that affect component proteins or the complex, are therapeutically or prophylactically administered to a human patient.

Preferably, suitable in vitro or in vivo assays are utilized to determine the effect of a specific therapeutic and whether its administration is indicated for treatment of the affected tissue or individual.

In various specific embodiments, in vitro assays can be carried out with representative cells of cell types involved in a patient's disorder, to determine if a therapeutic has a desired effect upon such cell types.

Compounds for use in therapy can be tested in suitable animal model systems prior to testing in humans, including, but not limited to, rats, mice, chicken, cows, monkeys, rabbits, etc. For in vivo testing, prior to administration to humans, any animal model system known in the art may be used. Additional descriptions and sources of therapeutics that can be used according to the invention are found in Sections 4.1 to 4.3 and 4.7 herein.

#### 4.4.1 GENE THERAPY

In a specific embodiment of the present invention, nucleic acids comprising a sequence encoding the component proteins, or a functional derivative thereof, are administered to modulate complex activity or formation by way of gene therapy. Gene therapy refers to therapy performed by the administration of a nucleic acid to a subject. In this embodiment of the present invention, the nucleic acid expresses its encoded protein(s) that mediates a therapeutic effect by modulating complex activity or formation. Any of the methods for gene therapy available in the art can be used according to the present invention. Exemplary methods are described below.

For general reviews of the methods of gene therapy, see Goldspiel et al., 1993, *Clinical Pharmacy* 12:488-505; Wu and Wu, 1991, *Biotherapy* 3:87-95; Tolstoshev, 1993, *Ann. Rev. Pharmacol. Toxicol.* 32:573-596; Mulligan, 1993, *Science* 260:926-932; Morgan and Anderson, 1993, *Ann. Rev. Biochem.* 62:191-217; and May, 1993, *TIBTECH* 11:155-215. Methods commonly known in the art of recombinant DNA technology which can be used are described in Ausubel et al., eds., 1993, *Current Protocols in Molecular Biology*, John Wiley & Sons, NY; and Kriegler, 1990, *Gene Transfer and Expression, A Laboratory Manual*, Stockton Press, NY.

In a preferred aspect, the therapeutic comprises a nucleic acid that is part of an expression vector that expresses one or more of the component proteins, or fragments or chimeric proteins thereof, in a suitable host. In particular, such a nucleic acid has a promoter operably linked to the protein coding region(s) (or, less preferably separate promoters linked to the separate coding regions separately), said promoter being inducible or constitutive, and optionally, tissue-specific. In another particular embodiment, a nucleic acid molecule is used in which the coding sequences, and any other desired sequences, are flanked by regions that promote homologous recombination at a desired site in the genome, thus providing for intra-chromosomal expression of the component protein nucleic acids (Koller and Smithies, 1989, *Proc. Natl. Acad. Sci. USA* 86:8932-8935; Zijlstra et al., 1989, *Nature* 342:435-438).

Delivery of the nucleic acid into a patient may be either direct, in which case the patient is directly exposed to the nucleic acid or nucleic acid-carrying vector, or indirect, in which case, cells are first transformed with the nucleic acid in vitro, then transplanted into the patient. These two approaches are known, respectively, as in vivo or ex vivo gene therapy.

In a specific embodiment, the nucleic acid is directly administered in vivo, where it is expressed to produce the encoded product. This can be accomplished by any of numerous methods known in the art, e.g., by constructing it as part of an appropriate nucleic acid expression vector and administering it so that it becomes intracellular, e.g., by infection using a defective or attenuated retroviral or other viral vector (U.S. Patent No. 4,980,286), or by direct injection of naked DNA, or by use of microparticle bombardment (e.g., a gene gun; Biolistic, Dupont), or coating with lipids or cell-surface receptors, or through use of transfecting agents, by encapsulation in liposomes, microparticles, or microcapsules, or by administering it in linkage to a peptide that is known to enter the nucleus, or by administering it in linkage to a ligand subject to receptor-mediated endocytosis that can be used to target cell types specifically expressing the receptors (e.g., Wu and Wu, 1987, *J. Biol. Chem.* 262:4429-4432), etc. In another embodiment, a nucleic acid-ligand complex can be formed in which the ligand comprises a fusogenic viral peptide that disrupts endosomes, allowing the nucleic acid to avoid lysosomal degradation. In yet another embodiment, the nucleic acid can be targeted in vivo for cell specific uptake and expression, by targeting a specific receptor (see, e.g., International Patent Publications WO 92/06180; WO 92/22635; WO 92/20316; WO 93/14188; and WO 93/20221. Alternatively, the nucleic acid can be introduced

intracellularly and incorporated within host cell DNA for expression, by homologous recombination (Koller and Smithies, 1989, *Proc. Natl. Acad. Sci. USA* 86:8932-8935; Zijlstra et al., 1989, *Nature* 342:435-438).

In a specific embodiment, a viral vector that contains the component protein encoding nucleic acids is used. For example, a retroviral vector can be used (Miller et al., 1993, *Meth. Enzymol.* 217:581-599). These retroviral vectors have been modified to delete retroviral sequences that are not necessary for packaging of the viral genome and integration into host cell DNA. The encoding nucleic acids to be used in gene therapy is/are cloned into the vector, which facilitates delivery of the gene into a patient. More detail about retroviral vectors can be found in Boesen et al., 1994, *Biotherapy* 6:291-302, which describes the use of a retroviral vector to deliver the *mdr1* gene to hematopoietic stem cells in order to make the stem cells more resistant to chemotherapy. Other references illustrating the use of retroviral vectors in gene therapy are Clowes et al., 1994, *J. Clin. Invest.* 93:644-651; Kiem et al., 1994, *Blood* 83:1467-1473; Salmons and Gunzberg, 1993, *Human Gene Therapy* 4:129-141; and Grossman and Wilson, 1993, *Curr. Opin. in Genetics and Devel.* 3:110-114.

Adenoviruses are other viral vectors that can be used in gene therapy. Adenoviruses are especially attractive vehicles for delivering genes to respiratory epithelia. Adenoviruses naturally infect respiratory epithelia where they cause a mild disease. Other targets for adenovirus-based delivery systems are the liver, the central nervous system, endothelial cells and muscle. Adenoviruses have the advantage of being capable of infecting non-dividing cells. Kozarsky and Wilson, 1993, *Curr. Opin. Genet. Devel.* 3:499-503, discuss adenovirus-based gene therapy. The use of adenovirus vectors to transfer genes to the respiratory epithelia of rhesus monkeys has been demonstrated by Bout et al., 1994, *Human Gene Therapy* 5:3-10. Other instances of the use of adenoviruses in gene therapy can be found in Rosenfeld et al., 1991, *Science* 252:431-434; Rosenfeld et al., 1992, *Cell* 68:143-155; and Mastrangeli et al., 1993, *J. Clin. Invest.* 91:225-234.

Adeno-associated virus (AAV) has also been proposed for use in gene therapy (Walsh et al., 1993, *Proc. Soc. Exp. Biol. Med.* 204:289-300).

Another approach to gene therapy involves transferring a gene into cells in tissue culture by methods such as electroporation, lipofection, calcium phosphate-mediated transfection, or viral infection. Usually, the method of transfer includes the transfer of a selectable marker to the cells. The cells are then placed under selection to isolate those

cells that have taken up and are expressing the transferred gene from these that have not. Those cells are then delivered to a patient.

In this embodiment, the nucleic acid is introduced into a cell prior to administration in vivo of the resulting recombinant cell. Such introduction can be carried out by any method known in the art including, but not limited to, transfection by electroporation, microinjection, infection with a viral or bacteriophage vector containing the nucleic acid sequences, cell fusion, chromosome-mediated gene transfer, microcell-mediated gene transfer, spheroplast fusion, etc. Numerous techniques are known in the art for the introduction of foreign genes into cells (see, e.g., Loeffler and Behr, 1993, *Meth. Enzymol.* 217:599-618; Cohen et al., 1993, *Meth. Enzymol.* 217:618-644; Cline, 1985, *Pharmac. Ther.* 29:69-92) and may be used in accordance with the present invention, provided that the necessary developmental and physiological functions of the recipient cells are not disrupted. The technique should provide for the stable transfer of the nucleic acid to the cell, so that the nucleic acid is expressible by the cell and preferably, is heritable and expressible by its cell progeny.

The resulting recombinant cells can be delivered to a patient by various methods known in the art. In a preferred embodiment, epithelial cells are injected, e.g., subcutaneously. In another embodiment, recombinant skin cells may be applied as a skin graft onto the patient. Recombinant blood cells (e.g., hematopoietic stem or progenitor cells) are preferably administered intravenously. The amount of cells envisioned for use depends on the desired effect, patient state, etc., and can be determined by one skilled in the art.

Cells into which a nucleic acid can be introduced for purposes of gene therapy encompass any desired, available cell type, and include but are not limited to epithelial cells, endothelial cells, keratinocytes, fibroblasts, muscle cells, hepatocytes, blood cells such as T lymphocytes, B lymphocytes, monocytes, macrophages, neutrophils, eosinophils, megakaryocytes, and granulocytes, various stem or progenitor cells, in particular hematopoietic stem or progenitor cells, e.g., as obtained from bone marrow, umbilical cord blood, peripheral blood, fetal liver, etc.

In a preferred embodiment, the cell used for gene therapy is autologous to the patient.

In an embodiment in which recombinant cells are used in gene therapy, a component protein encoding nucleic acid is/are introduced into the cells such that the gene or genes are expressible by the cells or their progeny, and the recombinant cells

are then administered in vivo for therapeutic effect. In a specific embodiment, stem or progenitor cells are used. Any stem and/or progenitor cells which can be isolated and maintained in vitro can potentially be used in accordance with this embodiment of the present invention. Such stem cells include but are not limited to hematopoietic stem cells (HSCs), stem cells of epithelial tissues such as the skin and the lining of the gut, embryonic heart muscle cells, liver stem cells (International Patent Publication WO 94/08598), and neural stem cells (Stemple and Anderson, 1992, Cell 71:973-985).

Epithelial stem cells (ESCs), or keratinocytes, can be obtained from tissues such as the skin and the lining of the gut by known procedures (Rheinwald, 1980, Meth. Cell Biol. 2A:229). In stratified epithelial tissue such as the skin, renewal occurs by mitosis of stem cells within the germinal layer, the layer closest to the basal lamina. Similarly, stem cells within the lining of the gut provide for a rapid renewal rate of this tissue. ESCs or keratinocytes obtained from the skin or lining of the gut of a patient or donor can be grown in tissue culture (Rheinwald, 1980, Meth. Cell Bio. 2A:229; Pittelkow and Scott, 1986, Mayo Clinic Proc. 61:771). If the ESCs are provided by a donor, a method for suppression of host versus graft reactivity (e.g., irradiation, or drug or antibody administration to promote moderate immunosuppression) can also be used.

With respect to hematopoietic stem cells (HSCs), any technique that provides for the isolation, propagation, and maintenance in vitro of HSCs can be used in this embodiment of the invention. Techniques by which this may be accomplished include (a) the isolation and establishment of HSC cultures from bone marrow cells isolated from the future host, or a donor, or (b) the use of previously established long-term HSC cultures, which may be allogeneic or xenogeneic. Non-autologous HSCs are used preferably in conjunction with a method of suppressing transplantation immune reactions between the future host and patient. In a particular embodiment of the present invention, human bone marrow cells can be obtained from the posterior iliac crest by needle aspiration (see, e.g., Kodo et al., 1984, J. Clin. Invest. 73: 1377-1384). In a preferred embodiment of the present invention, the HSCs can be made highly enriched or in substantially pure form. This enrichment can be accomplished before, during, or after long-term culturing, and can be done by any technique known in the art. Long-term cultures of bone marrow cells can be established and maintained by using, for example, modified Dexter cell culture techniques (Dexter et al., 1977, J. Cell Physiol. 91:335) or Witlock-Witte culture techniques (Witlock and Witte, 1982, Proc. Natl. Acad. Sci. USA 79:3608-3612).

In a specific embodiment, the nucleic acid to be introduced for purposes of gene therapy comprises an inducible promoter operably linked to the coding region, such that expression of the nucleic acid is controllable by controlling the presence or absence of the appropriate inducer of transcription.

Additional methods can be adapted for use to deliver a nucleic acid encoding the component proteins, or functional derivatives thereof, e.g., as described in Section 4.1, *supra*.

#### 4.4.2 USE OF ANTISENSE OLIGONUCLEOTIDES FOR SUPPRESSION OF PROTEIN COMPLEX FORMATION OR PROTEIN COMPLEX/PROTEIN ACTIVITY

In a specific embodiment of the present invention, protein complex activity and formation and protein activity is inhibited by use of antisense nucleic acids for the component proteins of the complex, that inhibit transcription and/or translation of their complementary sequence. The present invention provides the therapeutic or prophylactic use of nucleic acids of at least six nucleotides that are antisense to a gene or cDNA encoding a component protein, or a portion thereof. An "antisense" nucleic acid as used herein refers to a nucleic acid capable of hybridizing to a sequence-specific portion of a component protein RNA (preferably mRNA) by virtue of some sequence complementarity. The antisense nucleic acid may be complementary to a coding and/or noncoding region of a component protein mRNA. Such antisense nucleic acids that inhibit complex formation or activity have utility as therapeutics, and can be used in the treatment or prevention of disorders as described *supra*.

The antisense nucleic acids of the invention can be oligonucleotides that are double-stranded or single-stranded, RNA or DNA, or a modification or derivative thereof, which can be directly administered to a cell, or which can be produced intracellularly by transcription of exogenous, introduced sequences.

In another embodiment, the present invention is directed to a method for inhibiting the expression of component protein nucleic acid sequences, in a prokaryotic or eukaryotic cell, comprising providing the cell with an effective amount of a composition comprising an antisense nucleic acid of the component protein, or a derivative thereof, of the invention.

The antisense nucleic acids are of at least six nucleotides and are preferably oligonucleotides, ranging from 6 to about 200 nucleotides. In specific aspects, the oligonucleotide is at least 10 nucleotides, at least 15 nucleotides, at least 100 nucleotides, or at least 200 nucleotides. The oligonucleotides can be DNA or RNA or chimeric mixtures, or derivatives or modified versions thereof, and either single-stranded or double-stranded. The oligonucleotide can be modified at the base moiety, sugar moiety, or phosphate backbone. The oligonucleotide may include other appending groups such as peptides, agents facilitating transport across the cell membrane (see, e.g., Letsinger et al., 1989, Proc. Natl. Acad. Sci. USA 86:6553-6556; Lemaitre et al., 1987, Proc. Natl. Acad. Sci. USA 84:648-652; International Patent Publication No. WO 88/09810) or blood-brain barrier (see, e.g., International Patent Publication No. WO 89/10134), hybridization-triggered cleavage agents (see, e.g., Krol et al., 1988, BioTechniques 6:958-976), or intercalating agents (see, e.g., Zon, 1988, Pharm. Res. 5:539-549).

In a preferred aspect of the invention, an antisense oligonucleotide is provided, preferably as single-stranded DNA. The oligonucleotide may be modified at any position in its structure with constituents generally known in the art.

The antisense oligonucleotides may comprise at least one modified base moiety which is selected from the group including but not limited to 5-fluorouracil, 5-bromouracil, 5-chlorouracil, 5-iodouracil, hypoxanthine, xanthine, 4-acetylcytosine, 5-(carboxyhydroxymethyl)uracil, 5-carboxymethylaminomethyl-2-thio-uridine, 5-carboxymethylaminomethyluracil, dihydrouracil,  $\beta$ -D-galactosylqueosine, inosine, N6-isopentenyladenine, 1-methylguanine, 1-methylinosine, 2,2-dimethylguanine, 2-methyladenine, 2-methylguanine, 3-methylcytosine, 5-methylcytosine, N6-adenine, 7-methylguanine, 5-methylaminomethyluracil, 5-methoxyaminomethyl-2-thiouracil,  $\beta$ -D-mannosylqueosine, 5N-methoxycarboxymethyluracil, 5-methoxyuracil, 2-methyl-thio-N6-isopentenyladenine, uracil-5-oxyacetic acid (v), wybutoxosine, pseudouracil, queosine, 2-thiocytosine, 5-methyl-2-thiouracil, 2-thiouracil, 4-thiouracil, 5-methyluracil, uracil-5-oxyacetic acid methylester, uracil-5-oxyacetic acid (v), 5-methyl-2-thiouracil, 3-(3-amino-3-N-2-carboxypropyl) uracil, (acp3)w, and 2,6-diaminopurine.

In another embodiment, the oligonucleotide comprises at least one modified sugar moiety selected from the group including, but not limited to, arabinose, 2-fluoroarabinose, xylulose, and hexose.

In yet another embodiment, the oligonucleotide comprises at least one modified phosphate backbone selected from the group consisting of a phosphorothioate, a phosphorodithioate, a phosphoramidothioate, a phosphoramidate, a phosphordiamidate, a methylphosphonate, an alkyl phosphotriester, and a formacetal, or an analog of the foregoing.

In yet another embodiment, the oligonucleotide is a 2'- $\alpha$ -anomeric oligonucleotide. An  $\alpha$ -anomeric oligonucleotide forms specific double-stranded hybrids with complementary RNA in which, contrary to the usual  $\beta$ -units, the strands run parallel to each other (Gautier et al., 1987, Nucl. Acids Res. 15:6625-6641).

The oligonucleotide may be conjugated to another molecule, e.g., a peptide, hybridization-triggered cross-linking agent, transport agent, hybridization-triggered cleavage agent, etc.

Oligonucleotides of the invention may be synthesized by standard methods known in the art, e.g., by use of an automated DNA synthesizer (such as are commercially available from Biosearch, Applied Biosystems, etc.). As examples, phosphorothioate oligonucleotides may be synthesized by the method of Stein et al. (1988, Nucl. Acids Res. 16:3209), methylphosphonate oligonucleotides can be prepared by use of controlled pore glass polymer supports (Sarin et al., 1988, Proc. Natl. Acad. Sci. USA 85:7448-7451), etc.

In a specific embodiment, the antisense oligonucleotides comprise catalytic RNAs, or ribozymes (see, e.g., International Patent Publication No. WO 90/11364; Sarver et al., 1990, Science 247:1222-1225). In another embodiment, the oligonucleotide is a 2'-O-methylribonucleotide (Inoue et al., 1987, Nucl. Acids Res. 15:6131-6148), or a chimeric RNA-DNA analog (Inoue et al., 1987, FEBS Lett. 215:327-330).

In an alternative embodiment, the antisense nucleic acids of the invention are produced intracellularly by transcription from an exogenous sequence. For example, a vector can be introduced in vivo such that it is taken up by a cell, within which cell the vector or a portion thereof is transcribed, producing an antisense nucleic acid (RNA) of the invention. Such a vector would contain a sequence encoding the component protein. Such a vector can remain episomal or become chromosomally integrated, as long as it can be transcribed to produce the desired antisense RNA. Such vectors can be constructed by recombinant DNA technology methods standard in the art. Vectors can be plasmid, viral, or others known in the art to be capable of replication and expression in



mammalian cells. Expression of the sequences encoding the antisense RNAs can be by any promoter known in the art to act in mammalian, preferably human, cells. Such promoters can be inducible or constitutive. Such promoters include, but are not limited to, the SV40 early promoter region (Bernoist and Chambon, 1981, *Nature* 290:304-310), the promoter contained in the 3' long terminal repeat of Rous sarcoma virus (Yamamoto et al., 1980, *Cell* 22:787-797), the herpes thymidine kinase promoter (Wagner et al., 1981, *Proc. Natl. Acad. Sci. USA* 78:1441-1445), the regulatory sequences of the metallothionein gene (Brinster et al., 1982, *Nature* 296:39-42), etc.

The antisense nucleic acids of the invention comprise a sequence complementary to at least a portion of an RNA transcript of a component protein gene, preferably a human gene. However, absolute complementarity, although preferred, is not required. A sequence "complementary to at least a portion of an RNA," as referred to herein, means a sequence having sufficient complementarity to be able to hybridize with the RNA, forming a stable duplex; in the case of double-stranded antisense nucleic acids, a single strand of the duplex DNA may thus be tested, or triplex formation may be assayed. The ability to hybridize will depend on both the degree of complementarity and the length of the antisense nucleic acid. Generally, the longer the hybridizing nucleic acid, the more base mismatches with a component protein RNA it may contain and still form a stable duplex (or triplex, as the case may be). One skilled in the art can ascertain a tolerable degree of mismatch by use of standard procedures to determine the melting point of the hybridized complex.

The component protein antisense nucleic acids can be used to treat (or prevent) disorders of a cell type that expresses, or preferably overexpresses, a protein complex.

Cell types that express or overexpress component protein RNA can be identified by various methods known in the art. Such methods include, but are not limited to, hybridization with component protein-specific nucleic acids (e.g., by Northern blot hybridization, dot blot hybridization, or in situ hybridization), or by observing the ability of RNA from the cell type to be translated in vitro into the component protein by immunohistochemistry, Western blot analysis, ELISA, etc. In a preferred aspect, primary tissue from a patient can be assayed for protein expression prior to treatment, e.g., by immunocytochemistry, in situ hybridization, or any number of methods to detect protein or mRNA expression.

Pharmaceutical compositions of the invention (see Section 4.7, *infra*), comprising an effective amount of a protein component antisense nucleic acid in a pharmaceutically

acceptable carrier can be administered to a patient having a disease or disorder that is of a type that expresses or overexpresses a protein complex of the present invention.

The amount of antisense nucleic acid that will be effective in the treatment of a particular disorder or condition will depend on the nature of the disorder or condition, and can be determined by standard clinical techniques. Where possible, it is desirable to determine the antisense cytotoxicity in vitro, and then in useful animal model systems, prior to testing and use in humans.

In a specific embodiment, pharmaceutical compositions comprising antisense nucleic acids are administered via liposomes, microparticles, or microcapsules. In various embodiments of the invention, it may be useful to use such compositions to achieve sustained release of the antisense nucleic acids. In a specific embodiment, it may be desirable to utilize liposomes targeted via antibodies to specific identifiable central nervous system cell types (Leonetti et al., 1990, Proc. Natl. Acad. Sci. U.S.A. 87:2448-2451; Renneisen et al., 1990, J. Biol. Chem. 265:16337-16342).

#### 4.5 ASSAYS OF PROTEIN COMPLEXES/PROTEINS OF THE INVENTION AND DERIVATIVES AND ANALOGS THEREOF

The functional activity of a protein complex of the present invention, or a derivative, fragment or analog thereof or protein component thereof, can be assayed by various methods. Potential modulators (e.g., agonists and antagonists) of complex activity or formation, e.g., anti-complex antibodies and antisense nucleic acids, can be assayed for the ability to modulate complex activity or formation.

In one embodiment of the present invention, where one is assaying for the ability to bind or compete with a wild-type complex for binding to an anti-complex antibody, various immunoassays known in the art can be used, including but not limited to competitive and non-competitive assay systems using techniques such as radioimmunoassay, ELISA (enzyme linked immunosorbent assay), "sandwich" immunoassays, immunoradiometric assays, gel diffusion precipitin reactions, immunodiffusion assays, in situ immunoassays (using colloidal gold, enzyme or radioisotope labels), western blot analysis, precipitation reactions, agglutination assays (e.g., gel agglutination assays, hemagglutination assays), complement fixation assays, immunofluorescence assays, protein A assays, immunoelectrophoresis assays, etc. In

one embodiment, antibody binding is detected by detecting a label on the primary antibody. In another embodiment, the primary antibody is detected by detecting binding of a secondary antibody or reagent to the primary antibody. In a further embodiment, the secondary antibody is labeled. Many means are known in the art for detecting binding in an immunoassay and are within the scope of the present invention.

The expression of the component protein genes (both endogenous and those expressed from cloned DNA containing the genes) can be detected using techniques known in the art, including but not limited to Southern hybridization (Southern, 1975, J. Mol. Biol. 98:503-517), northern hybridization (see, e.g., Freeman et al., 1983, Proc. Natl. Acad. Sci. USA 80:4094-4098), restriction endonuclease mapping (Sambrook et al., 1989, Molecular Cloning, A Laboratory Manual, 2<sup>nd</sup> Ed. Cold Spring Harbor Laboratory Press, New York), RNase protection assays (Current Protocols in Molecular Biology, John Wiley and Sons, New York, 1997), DNA sequence analysis, and polymerase chain reaction amplification (PCR; U.S. Patent Nos. 4,683,202, 4,683,195, and 4,889,818; Gyllenstein et al., 1988, Proc. Natl. Acad. Sci. USA 85:7652-7657; Ochman et al., 1988, Genetics 120:621-623; Loh et al., 1989, Science 243:217-220) followed by Southern hybridization with probes specific for the component protein genes, in various cell types. Methods of amplification other than PCR commonly known in the art can be employed. In one embodiment, Southern hybridization can be used to detect genetic linkage of component protein gene mutations to physiological or pathological states. Various cell types, at various stages of development, can be characterized for their expression of component proteins at the same time and in the same cells. The stringency of the hybridization conditions for northern or Southern blot analysis can be manipulated to ensure detection of nucleic acids with the desired degree of relatedness to the specific probes used. Modifications to these methods and other methods commonly known in the art can be used.

Derivatives (e.g., fragments), homologs and analogs of one component protein can be assayed for binding to another component protein in the same complex by any method known in the art, for example the modified yeast matrix mating test described in Section 4.6.1 *infra*, immunoprecipitation with an antibody that binds to the component protein complexed with other component proteins in the same complex, followed by size fractionation of the immunoprecipitated proteins (e.g., by denaturing or nondenaturing polyacrylamide gel electrophoresis), Western blot analysis, etc.

One embodiment of the invention provides a method for screening a derivative, homolog or analog of a component protein for biological activity comprising contacting said derivative, homolog or analog of the component protein with the other component proteins in the same complex; and detecting the formation of a complex between said derivative, homolog or analog of the component protein and the other component proteins; wherein detecting formation of said complex indicates that said derivative, homolog or analog of has biological (e.g., binding) activity.

The invention also provides methods of modulating the activity of a component protein that can participate in a protein complex by administration of a binding partner of that protein or derivative, homolog or analog thereof.

In a specific embodiment of the present invention, a protein complex of the present invention is administered to treat or prevent a disease or disorder, since the complex and/or component proteins have been implicated in the disease and disorder. Accordingly, a protein complex or a derivative, homolog, analog or fragment thereof, nucleic acids encoding the component proteins, anti-complex antibodies, and other modulators of protein complex activity, can be tested for activity in treating or preventing a disease or disorder in in vitro and in vivo assays.

In one embodiment, a therapeutic of the invention can be assayed for activity in treating or preventing a disease by contacting cultured cells that exhibit an indicator of the disease in vitro, with the therapeutic, and comparing the level of said indicator in the cells contacted with the therapeutic, with said level of said indicator in cells not so contacted, wherein a lower level in said contacted cells indicates that the therapeutic has activity in treating or preventing the disease.

In another embodiment of the invention, a therapeutic of the invention can be assayed for activity in treating or preventing a disease by administering the therapeutic to a test animal that is predisposed to develop symptoms of a disease, and measuring the change in said symptoms of the disease after administration of said therapeutic, wherein a reduction in the severity of the symptoms of the disease or prevention of the symptoms of the disease indicates that the therapeutic has activity in treating or preventing the disease. Such a test animal can be any one of a number of animal models known in the art for disease. These animal models are well known in the art. These animal models include, but are not limited to those which are listed in the section 4.6 (supra) as exemplary animal models to study any of the complexes provided in the invention.

#### **4.6 SCREENING FOR MODULATORS OF THE PROTEIN COMPLEXES/PROTEINS OF THE INVENTION**

A complex of the present invention, the component proteins of the complex and nucleic acids encoding the component proteins, as well as derivatives and fragments of the amino and nucleic acids, can be used to screen for compounds that bind to, or modulate the amount of, activity of, or protein component composition of, said complex, and thus, have potential use as modulators, i.e., agonists or antagonists, of complex activity, and/or complex formation, i.e., the amount of complex formed, and/or protein component composition of the complex.

Thus, the present invention is also directed to methods for screening for molecules that bind to, or modulate the function of, amount of, activity of, formation of or protein component composition of, a complex of the present invention. In one embodiment of the invention, the method for screening for a molecule that modulates directly or indirectly the function, activity or formation of a complex of the present invention comprises exposing said complex, or a cell or organism containing the complex machinery, to one or more candidate molecules under conditions conducive to modulation; and determining the amount of, the biochemical activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.

In a further specific embodiment, a modulation of the formation process of a complex can be determined.

Such a modulation can either be a change in the typical time course of its formation or a change in the typical steps leading to the formation of the complete complex.

Such changes can for example be detected by analysing and comparing the process of complex formation in untreated wild type cells of a particular type and/or cells showing or having the predisposition to develop a certain disease phenotype and/or cells which have been treated with particular conditions and/or particular agents in a particular situation. Methods to study such changes in time course are well known in the art and include for example Western-blot analysis of the proteins in the complex isolated at different steps of its formation.

Furthermore an aberrant intracellular localization of the protein complex and/or an aberrant transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or a gene dependent on the complex can serve as a marker for a disease and thus have diagnostic utility for any disease which is caused by an aberrant activity, function, composition or formation of the complex of the invention.

Methods to study the intracellular localization are well known in the art and include, but are not limited to immunofluorescence analysis using antibodies specific for components of the protein. Preferentially, double-stainings including staining of other cellular structures are being used to facilitate the detection of the intracellular localization. Methods to analyse the transcription levels of a gene dependent on the complex are also well known in the art and include Northern blot analysis, quantitative PCR etc. The abundance of proteins dependent on the protein can be analyzed as described supra. Methods to study changes in the activity of proteins dependent on complex depend on the protein. The choice of such methods will be apparent to any person skilled in the art.

In another embodiment, the present invention further relates to a process for the identification and/or preparation of an effector of the complex comprising the step of bringing into contact a product of any of claims 1 to 8 with a compound, a mixture or a library of compounds and determining whether the compound or a certain compound of the mixture or library binds to the product and/or effects the products biological activity and optionally further purifying the compound positively tested as effector.

In another embodiment, the present invention is directed to a method for screening for a molecule that binds a protein complex of the present invention comprising exposing said complex, or a cell or organism containing the complex

machinery, to one or more candidate molecules; and determining whether said complex is bound by any of said candidate molecules. Such screening assays can be carried out using cell-free and cell-based methods that are commonly known in the art *in vitro*, *in vivo* or *ex vivo*. For example, an isolated complex can be employed, or a cell can be contacted with the candidate molecule and the complex can be isolated from such contacted cells and the isolated complex can be assayed for activity or component composition. In another example, a cell containing the complex can be contacted with the candidate molecule and the levels of the complex in the contacted cell can be measured. Additionally, such assays can be carried out in cells recombinantly expressing a component protein from the fourth column of table 1, or a functionally active fragment or functionally active derivative thereof, and a component protein from fifth column of table 1, or a functionally active fragment or functionally active derivative thereof. Additionally, such assays can also be carried out in cells recombinantly expressing all component proteins from the group of proteins in the fifth column of table 1.

For example, assays can be carried out using recombinant cells expressing the protein components of a complex, to screen for molecules that bind to, or interfere with, or promote complex activity or formation. In preferred embodiments, polypeptide derivatives that have superior stabilities but retain the ability to form a complex (e.g., one or more component proteins modified to be resistant to proteolytic degradation in the binding assay buffers, or to be resistant to oxidative degradation), are used to screen for modulators of complex activity or formation. Such resistant molecules can be generated, e.g., by substitution of amino acids at proteolytic cleavage sites, the use of chemically derivatized amino acids at proteolytic susceptible sites, and the replacement of amino acid residues subject to oxidation, i.e. methionine and cysteine.

A particular aspect of the present invention relates to identifying molecules that inhibit or promote formation or degradation of a complex of the present invention, e.g., using the method described for isolating the complex and identifying members of the complex using the TAP assay described in Section 4, *infra*, and in WO 00/09716 and Rigaut et al., 1999, Nature Biotechnol. 17:1030-1032, which are each incorporated by reference in their entirety. TNRF1

In another embodiment of the invention, a modulator is identified by administering a candidate molecule to a transgenic non-human animal expressing the complex component proteins from promoters that are not the native promoters of the respective

proteins, more preferably where the candidate molecule is also recombinantly expressed in the transgenic non-human animal. Alternatively, the method for identifying such a modulator can be carried out in vitro, preferably with a purified complex, and a purified candidate molecule.

Agents/molecules (candidate molecules) to be screened can be provided as mixtures of a limited number of specified compounds, or as compound libraries, peptide libraries and the like. Agents/molecules to be screened may also include all forms of antisera, antisense nucleic acids, etc., that can modulate complex activity or formation. Exemplary candidate molecules and libraries for screening are set forth in Section 4.6.1, *infra*.

Screening the libraries can be accomplished by any of a variety of commonly known methods. See, e.g., the following references, which disclose screening of peptide libraries: Parmley and Smith, 1989, *Adv. Exp. Med. Biol.* 251:215-218; Scott and Smith, 1990, *Science* 249:386-390; Fowlkes et al., 1992, *BioTechniques* 13:422-427; Oldenburg et al., 1992, *Proc. Natl. Acad. Sci. USA* 89:5393-5397; Yu et al., 1994, *Cell* 76:933-945; Staudt et al., 1988, *Science* 241:577-580; Bock et al., 1992, *Nature* 355:564-566; Tuerk et al., 1992, *Proc. Natl. Acad. Sci. USA* 89:6988-6992; Ellington et al., 1992, *Nature* 355:850-852; U.S. Patent No. 5,096,815, U.S. Patent No. 5,223,409, and U.S. Patent No. 5,198,346, all to Ladner et al.; Rebar and Pabo, 1993, *Science* 263:671-673; and International Patent Publication No. WO 94/18318.

In a specific embodiment, screening can be carried out by contacting the library members with a complex immobilized on a solid phase, and harvesting those library members that bind to the protein (or encoding nucleic acid or derivative). Examples of such screening methods, termed "panning" techniques, are described by way of example in Parmley and Smith, 1988, *Gene* 73:305-318; Fowlkes et al., 1992, *BioTechniques* 13:422-427; International Patent Publication No. WO 94/18318; and in references cited hereinabove.

In a specific embodiment, fragments and/or analogs of protein components of a complex, especially peptidomimetics, are screened for activity as competitive or non-competitive inhibitors of complex formation (amount of complex or composition of complex) or activity in the cell, which thereby inhibit complex activity or formation in the cell.

In one embodiment, agents that modulate (i.e., antagonize or agonize) complex activity or formation can be screened for using a binding inhibition assay, wherein agents



are screened for their ability to modulate formation of a complex under aqueous, or physiological, binding conditions in which complex formation occurs in the absence of the agent to be tested. Agents that interfere with the formation of complexes of the invention are identified as antagonists of complex formation. Agents that promote the formation of complexes are identified as agonists of complex formation. Agents that completely block the formation of complexes are identified as inhibitors of complex formation.

Methods for screening may involve labeling the component proteins of the complex with radioligands (e.g.,  $^{125}\text{I}$  or  $^3\text{H}$ ), magnetic ligands (e.g., paramagnetic beads covalently attached to photobiotin acetate), fluorescent ligands (e.g., fluorescein or rhodamine), or enzyme ligands (e.g., luciferase or  $\beta$ -galactosidase). The reactants that bind in solution can then be isolated by one of many techniques known in the art, including but not restricted to, co-immunoprecipitation of the labeled complex moiety using antisera against the unlabeled binding partner (or labeled binding partner with a distinguishable marker from that used on the second labeled complex moiety), immunoaffinity chromatography, size exclusion chromatography, and gradient density centrifugation. In a preferred embodiment, the labeled binding partner is a small fragment or peptidomimetic that is not retained by a commercially available filter. Upon binding, the labeled species is then unable to pass through the filter, providing for a simple assay of complex formation.

Methods commonly known in the art are used to label at least one of the component members of the complex. Suitable labeling methods include, but are not limited to, radiolabeling by incorporation of radiolabeled amino acids, e.g.,  $^3\text{H}$ -leucine or  $^{35}\text{S}$ -methionine, radiolabeling by post-translational iodination with  $^{125}\text{I}$  or  $^{131}\text{I}$  using the chloramine T method, Bolton-Hunter reagents, etc., or labeling with  $^{32}\text{P}$  using phosphorylase and inorganic radiolabeled phosphorous, biotin labeling with photobiotin-acetate and sunlamp exposure, etc. In cases where one of the members of the complex is immobilized, e.g., as described infra, the free species is labeled. Where neither of the interacting species is immobilized, each can be labeled with a distinguishable marker such that isolation of both moieties can be followed to provide for more accurate quantification, and to distinguish the formation of homomeric from heteromeric complexes. Methods that utilize accessory proteins that bind to one of the modified interactants to improve the sensitivity of detection, increase the stability of the complex, etc., are provided.

Typical binding conditions are, for example, but not by way of limitation, in an aqueous salt solution of 10-250 mM NaCl, 5-50 mM Tris-HCl, pH 5-8, and 0.5% Triton X-100 or other detergent that improves specificity of interaction. Metal chelators and/or divalent cations may be added to improve binding and/or reduce proteolysis. Reaction temperatures may include 4, 10, 15, 22, 25, 35, or 42 degrees Celsius, and time of incubation is typically at least 15 seconds, but longer times are preferred to allow binding equilibrium to occur. Particular complexes can be assayed using routine protein binding assays to determine optimal binding conditions for reproducible binding.

The physical parameters of complex formation can be analyzed by quantification of complex formation using assay methods specific for the label used, e.g., liquid scintillation counting for radioactivity detection, enzyme activity for enzyme-labeled moieties, etc. The reaction results are then analyzed utilizing Scatchard analysis, Hill analysis, and other methods commonly known in the arts (see, e.g., *Proteins, Structures, and Molecular Principles*, 2<sup>nd</sup> Edition (1993) Creighton, Ed., W.H. Freeman and Company, New York).

In a second common approach to binding assays, one of the binding species is immobilized on a filter, in a microtiter plate well, in a test tube, to a chromatography matrix, etc., either covalently or non-covalently. Proteins can be covalently immobilized using any method well known in the art, for example, but not limited to the method of Kadonaga and Tjian, 1986, *Proc. Natl. Acad. Sci. USA* 83:5889-5893, i.e., linkage to a cyanogen-bromide derivatized substrate such as CNBr-Sepharose 4B (Pharmacia). Where needed, the use of spacers can reduce steric hindrance by the substrate. Non-covalent attachment of proteins to a substrate include, but are not limited to, attachment of a protein to a charged surface, binding with specific antibodies, binding to a third unrelated interacting protein, etc.

Assays of agents (including cell extracts or a library pool) for competition for binding of one member of a complex (or derivatives thereof) with another member of the complex labeled by any means (e.g., those means described above) are provided to screen for competitors or enhancers of complex formation.

In specific embodiments, blocking agents to inhibit non-specific binding of reagents to other protein components, or absorptive losses of reagents to plastics, immobilization matrices, etc., are included in the assay mixture. Blocking agents include, but are not restricted to bovine serum albumin,  $\beta$ -casein, nonfat dried milk, Denhardt's reagent, Ficoll, polyvinylpyrrolidone, nonionic detergents (NP40, Triton X-100, Tween 20,

Tween 80, etc.), ionic detergents (e.g., SDS, LDS, etc.), polyethylene glycol, etc. Appropriate blocking agent concentrations allow complex formation.

After binding is performed, unbound, labeled protein is removed in the supernatant, and the immobilized protein retaining any bound, labeled protein is washed extensively. The amount of bound label is then quantified using standard methods in the art to detect the label as described, *supra*.

In another specific embodiments screening for modulators of the protein complexes/protein as provided herein can be carried out by attaching those and/or the antibodies as provided herein to a solid carrier. In a further specific embodiment, the invention relates to an array of said molecules.

The preparation of such an array containing different types of proteins, including antibodies) is well known in the art and is apparent to a person skilled in the art (see e.g. Ekins et al., 1989, *J. Pharm. Biomed. Anal.* 7:155-168; Mitchell et al. 2002, *Nature Biotechnol.* 20:225-229; Petricoin et al., 2002, *Lancet* 359:572-577; Templin et al., 2001, *Trends Biotechnol.* 20:160-166; Wilson and Nock, 2001, *Curr. Opin. Chem. Biol.* 6:81-85; Lee et al., 2002 *Science* 295:1702-1705; MacBeath and Schreiber, 2000, *Science* 289:1760; Blawas and Reichert, 1998, *Biomaterials* 19:595; Kane et al., 1999, *Biomaterials* 20:2363; Chen et al., 1997, *Science* 276:1425; Vaugham et al., 1996, *Nature Biotechnol.* 14:309-314; Mahler et al., 1997, *Immunotechnology* 3:31-43; Roberts et al., 1999, *Curr. Opin. Chem. Biol.* 3:268-273; Nord et al., 1997, *Nature Biotechnol.* 15:772-777; Nord et al., 2001, *Eur. J. Biochem.* 268:4269-4277; Brody and Gold, 2000, *Rev. Mol. Biotechnol.* 74:5-13; Karlstroem and Nygren, 2001, *Anal. Biochem.* 295:22-30; Nelson et al., 2000, *Electrophoresis* 21:1155-1163; Honore et al., 2001, *Expert Rev. Mol. Diagn.* 3:265-274; Albala, 2001, *Expert Rev. Mol. Diagn.* 2:145-152, Figeys and Pinto, 2001, *Electrophoresis* 2:208-216 and references in the publications listed here).

Complexes can be attached to an array by different means as will be apparent to a person skilled in the art. Complexes can for example be added to the array via a TAP-tag (as described in WO/0009716 and in Rigaut et al., 1999, *Nature Biotechnol.* 10:1030-1032) after the purification step or by another suitable purification scheme as will be apparent to a person skilled in the art.

Optionally, the proteins of the complex can be cross-linked to enhance the stability of the complex. Different methods to cross-link proteins are well known in the art. Reactive end-groups of cross-linking agents include but are not limited to -COOH, -SH, -NH<sub>2</sub> or N-oxy-succinamate.

The spacer of the cross-linking agent should be chosen with respect to the size of the complex to be cross-linked. For small protein complexes, comprising only a few proteins, relatively short spacers are preferable in order to reduce the likelihood of cross-linking separate complexes in the reaction mixture. For larger protein complexes, additional use of larger spacers is preferable in order to facilitate cross-linking between proteins within the complex.

It is preferable to check the success-rate of cross-linking before linking the complex to the carrier.

As will be apparent to a person skilled in the art, the optimal rate of cross-linking need to be determined on a case by case basis. This can be achieved by methods well known in the art, some of which are exemplary described below.

A sufficient rate of cross-linking can be checked f.e. by analysing the cross-linked complex vs. a non-cross-linked complex on a denaturing protein gel.

If cross-linking has been performed successfully, the proteins of the complex are expected to be found in the same lane, whereas the proteins of the non-cross-linked complex are expected to be separated according to their individual characteristics. Optionally the presence of all proteins of the complex can be further checked by peptide-sequencing of proteins in the respective bands using methods well known in the art such as mass spectrometry and/or Edman degradation.

In addition, a rate of crosslinking which is too high should also be avoided. If cross-linking has been carried out too extensively, there will be an increasing amount of cross-linking of the individual protein complex, which potentially interferes with a screening for potential binding partners and/or modulators etc. using the arrays.

The presence of such structures can be determined by methods well known in the art and include e.g. gel-filtration experiments comparing the gel filtration profile solutions containing cross-linked complexes vs. uncross-linked complexes.

Optionally, functional assays as will be apparent to a person skilled in the art, some of which are exemplarily provided herein, can be performed to check the integrity of the complex.

Alternatively, members of the protein complex can be expressed as a single fusion protein and coupled to the matrix as will be apparent to a person skilled in the art.

Optionally, the attachment of the complex or proteins or antibody as outlined above can be further monitored by various methods apparent to a person skilled in the art. Those include, but are not limited to surface plasmon resonance (see e.g. McDonnel, 2001, *Curr. Opin. Chem. Biol.* 5:572-577; Lee, 2001, *Trends Biotechnol.* 19:217-222; Weinberger et al., 2000, 1:395-416; Pearson et al., 2000, *Ann. Clin. Biochem.* 37:119-145; Vely et al., 2000, *Methods Mol. Biol.* 121:313-321; Slepak, 2000, *J. Mol. Recognit.* 13:20-26.

Exemplary assays useful for measuring transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Fe65-complex include but are not limited to those described in Cao X et al., 2001, *Science*, 293:115-20.

Exemplary assays useful for measuring the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Fe65-complex include but are not limited to those described in Vassar R et al., 1999, *Science*, 286:735-41.

Exemplary assays useful for measuring the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Fe65-complex include but are not limited to those described in Yan R et al., 1999, *Nature*, 402:533-7.

Exemplary assays useful for measuring the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting of the Fe65-complex include but are not limited to those described in Tian Gaochao et al., 2002, *J Biol Chem*, 277:31499-505.

Exemplary assays useful for measuring the transactivation of reporter genes by APP-Gal4/VP16 (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the X11b-complex include but are not limited to those described in Biederer Thomas et al., 2002, *J Neurosci*, 22:7340-51.

Exemplary assays useful for measuring the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the X11b-complex include but are not limited to those described in Vassar R et al., 1999, Science, 286:735-41.

Exemplary assays useful for measuring the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the X11b-complex include but are not limited to those described in Yan R et al., 1999, Nature, 402:533-7.

Exemplary assays useful for measuring the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the X11b-complex include but are not limited to those described in Tian Gaochao et al., 2002, J Biol Chem, 277:31499-505.

Exemplary assays useful for measuring the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the PSEN2 -complex include but are not limited to those described in Vassar R et al., 1999, Science, 286:735-41.

Exemplary assays useful for measuring the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the PSEN2 -complex include but are not limited to those described in Yan R et al., 1999, Nature, 402:533-7.

Exemplary assays useful for measuring the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting of the PSEN2 -complex include but are not limited to those described in Tian Gaochao et al., 2002, J Biol Chem, 277:31499-505.

Exemplary assays useful for measuring transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the

PSEN2 -complex include but are not limited to those described in Cao X et al., 2001, Science, 293:115-20.

Exemplary assays useful for measuring the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Nicastrin-complex include but are not limited to those described in Vassar R et al., 1999, Science, 286:735-41.

Exemplary assays useful for measuring the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Nicastrin-complex include but are not limited to those described in Yan R et al., 1999, Nature, 402:533-7.

Exemplary assays useful for measuring the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting of the Nicastrin-complex include but are not limited to those described in Tian Gaochao et al., 2002, J Biol Chem, 277:31499-505.

Exemplary assays useful for measuring transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Nicastrin-complex include but are not limited to those described in Cao X et al., 2001, Science, 293:115-20.

Exemplary assays useful for measuring the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Aph-1a-complex include but are not limited to those described in Vassar R et al., 1999, Science, 286:735-41.

Exemplary assays useful for measuring the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Aph-1a-complex include but are not limited to those described in Yan R et al., 1999, Nature, 402:533-7.

Exemplary assays useful for measuring the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the

expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting of the Aph-1a-complex include but are not limited to those described in Tian Gaochao et al., 2002, J Biol Chem, 277:31499-505.

Exemplary assays useful for measuring transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Aph-1a-complex include but are not limited to those described in Cao X et al., 2001, Science, 293:115-20.

Exemplary assays useful for measuring the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Pen-2-complex include but are not limited to those described in Vassar R et al., 1999, Science, 286:735-41.

Exemplary assays useful for measuring the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Pen-2-complex include but are not limited to those described in Yan R et al., 1999, Nature, 402:533-7.

Exemplary assays useful for measuring the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting of the Pen-2-complex include but are not limited to those described in Tian Gaochao et al., 2002, J Biol Chem, 277:31499-505.

Exemplary assays useful for measuring transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Pen-2-complex include but are not limited to those described in Cao X et al., 2001, Science, 293:115-20.

Exemplary assays useful for measuring the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the APP695SW-complex include but are not limited to those described in Vassar R et al., 1999, Science, 286:735-41.



Exemplary assays useful for measuring the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the APP695SW-complex include but are not limited to those described in Yan R et al., 1999, *Nature*, 402:533-7.

Exemplary assays useful for measuring the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting of the APP695SW-complex include but are not limited to those described in Tian Gaochao et al., 2002, *J Biol Chem*, 277:31499-505.

Exemplary assays useful for measuring transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the APP695SW-complex include but are not limited to those described in Cao X et al., 2001, *Science*, 293:115-20.

Exemplary assays useful for measuring the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the APP-C99 -complex include but are not limited to those described in Vassar R et al., 1999, *Science*, 286:735-41.

Exemplary assays useful for measuring the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the APP-C99 -complex include but are not limited to those described in Yan R et al., 1999, *Nature*, 402:533-7.

Exemplary assays useful for measuring the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting of the APP-C99 -complex include but are not limited to those described in Tian Gaochao et al., 2002, *J Biol Chem*, 277:31499-505.

Exemplary assays useful for measuring transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the APP-

C99 -complex include but are not limited to those described in Cao X et al., 2001, Science, 293:115-20.

Exemplary assays useful for measuring the phosphorylation of tau proteins in vitro or in cells (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Tau-complex include but are not limited to those described in Drewes G et al., 1997, Cell, 89:297-308.

Exemplary assays useful for measuring the aggregation of tau proteins into filaments or tangles in vitro or in cells (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Tau-complex include but are not limited to those described in Barghorn S et al., 2000, Biochemistry, 39:11714-21.

#### 4.6.1 CANDIDATE MOLECULES

Any molecule known in the art can be tested for its ability to modulate (increase or decrease) the amount of, activity of, or protein component composition of a complex of the present invention as detected by a change in the amount of, activity of, or protein component composition of, said complex. By way of example, a change in the amount of the complex can be detected by detecting a change in the amount of the complex that can be isolated from a cell expressing the complex machinery. For identifying a molecule that modulates complex activity, candidate molecules can be directly provided to a cell expressing the complex machinery, or, in the case of candidate proteins, can be provided by providing their encoding nucleic acids under conditions in which the nucleic acids are recombinantly expressed to produce the candidate proteins within the cell expressing the complex machinery, the complex is then isolated from the cell and the isolated complex is assayed for activity using methods well known in the art, not limited to those described, supra.

This embodiment of the invention is well suited to screen chemical libraries for molecules which modulate, e.g., inhibit, antagonize, or agonize, the amount of, activity of, or protein component composition of the complex. The chemical libraries can be peptide libraries, peptidomimetic libraries, chemically synthesized libraries, recombinant,

e.g., phage display libraries, and in vitro translation-based libraries, other non-peptide synthetic organic libraries, etc.

Exemplary libraries are commercially available from several sources (ArQule, Tripos/PanLabs, ChemDesign, Pharmacopoeia). In some cases, these chemical libraries are generated using combinatorial strategies that encode the identity of each member of the library on a substrate to which the member compound is attached, thus allowing direct and immediate identification of a molecule that is an effective modulator. Thus, in many combinatorial approaches, the position on a plate of a compound specifies that compound's composition. Also, in one example, a single plate position may have from 1-20 chemicals that can be screened by administration to a well containing the interactions of interest. Thus, if modulation is detected, smaller and smaller pools of interacting pairs can be assayed for the modulation activity. By such methods, many candidate molecules can be screened.

Many diversity libraries suitable for use are known in the art and can be used to provide compounds to be tested according to the present invention. Alternatively, libraries can be constructed using standard methods. Chemical (synthetic) libraries, recombinant expression libraries, or polysome-based libraries are exemplary types of libraries that can be used.

The libraries can be constrained or semirigid (having some degree of structural rigidity), or linear or nonconstrained. The library can be a cDNA or genomic expression library, random peptide expression library or a chemically synthesized random peptide library, or non-peptide library. Expression libraries are introduced into the cells in which the assay occurs, where the nucleic acids of the library are expressed to produce their encoded proteins.

In one embodiment, peptide libraries that can be used in the present invention may be libraries that are chemically synthesized in vitro. Examples of such libraries are given in Houghten et al., 1991, *Nature* 354:84-86, which describes mixtures of free hexapeptides in which the first and second residues in each peptide were individually and specifically defined; Lam et al., 1991, *Nature* 354:82-84, which describes a "one bead, one peptide" approach in which a solid phase split synthesis scheme produced a library of peptides in which each bead in the collection had immobilized thereon a single, random sequence of amino acid residues; Medynski, 1994, *Bio/Technology* 12:709-710, which describes split synthesis and T-bag synthesis methods; and Gallop et al., 1994, *J. Med. Chem.* 37:1233-1251. Simply by way of other examples, a combinatorial library

may be prepared for use, according to the methods of Ohlmeyer et al., 1993, Proc. Natl. Acad. Sci. USA 90:10922-10926; Erb et al., 1994, Proc. Natl. Acad. Sci. USA 91:11422-11426; Houghten et al., 1992, Biotechniques 13:412; Jayawickreme et al., 1994, Proc. Natl. Acad. Sci. USA 91:1614-1618; or Salmon et al., 1993, Proc. Natl. Acad. Sci. USA 90:11708-11712. PCT Publication No. WO 93/20242 and Brenner and Lerner, 1992, Proc. Natl. Acad. Sci. USA 89:5381-5383 describe "encoded combinatorial chemical libraries," that contain oligonucleotide identifiers for each chemical polymer library member.

In a preferred embodiment, the library screened is a biological expression library that is a random peptide phage display library, where the random peptides are constrained (e.g., by virtue of having disulfide bonding).

Further, more general, structurally constrained, organic diversity (e.g., nonpeptide) libraries, can also be used. By way of example, a benzodiazepine library (see e.g., Bunin et al., 1994, Proc. Natl. Acad. Sci. USA 91:4708-4712) may be used.

Conformationally constrained libraries that can be used include but are not limited to those containing invariant cysteine residues which, in an oxidizing environment, cross-link by disulfide bonds to form cystines, modified peptides (e.g., incorporating fluorine, metals, isotopic labels, are phosphorylated, etc.), peptides containing one or more non-naturally occurring amino acids, non-peptide structures, and peptides containing a significant fraction of  $\gamma$ -carboxyglutamic acid.

Libraries of non-peptides, e.g., peptide derivatives (for example, that contain one or more non-naturally occurring amino acids) can also be used. One example of these are peptoid libraries (Simon et al., 1992, Proc. Natl. Acad. Sci. USA 89:9367-9371). Peptoids are polymers of non-natural amino acids that have naturally occurring side chains attached not to the  $\alpha$  carbon but to the backbone amino nitrogen. Since peptoids are not easily degraded by human digestive enzymes, they are advantageously more easily adaptable to drug use. Another example of a library that can be used, in which the amide functionalities in peptides have been permethylated to generate a chemically transformed combinatorial library, is described by Ostresh et al., 1994, Proc. Natl. Acad. Sci. USA 91:11138-11142).

The members of the peptide libraries that can be screened according to the invention are not limited to containing the 20 naturally occurring amino acids. In particular, chemically synthesized libraries and polysome based libraries allow the use of amino acids in addition to the 20 naturally occurring amino acids (by their inclusion in the

precursor pool of amino acids used in library production). In specific embodiments, the library members contain one or more non-natural or non-classical amino acids or cyclic peptides. Non-classical amino acids include but are not limited to the D-isomers of the common amino acids,  $\gamma$ -amino isobutyric acid, 4-aminobutyric acid, Abu, 2-amino butyric acid;  $\gamma$ -Abu,  $\gamma$ -Ahx, 6-amino hexanoic acid; Aib, 2-amino isobutyric acid; 3-amino propionic acid; ornithine; norleucine; norvaline, hydroxyproline, sarcosine, citrulline, cysteic acid, t-butylglycine, t-butylalanine, phenylglycine, cyclohexylalanine,  $\beta$ -alanine, designer amino acids such as  $\beta$ -methyl amino acids,  $\gamma$ -methyl amino acids, N-methyl amino acids, fluoro-amino acids and amino acid analogs in general. Furthermore, the amino acid can be D (dextrorotary) or L (levorotary).

In a specific embodiment, fragments and/or analogs of complexes of the invention, or protein components thereof, especially peptidomimetics, are screened for activity as competitive or non-competitive inhibitors of complex activity or formation.

In another embodiment of the present invention, combinatorial chemistry can be used to identify modulators of a the complexes. Combinatorial chemistry is capable of creating libraries containing hundreds of thousands of compounds, many of which may be structurally similar. While high throughput screening programs are capable of screening these vast libraries for affinity for known targets, new approaches have been developed that achieve libraries of smaller dimension but which provide maximum chemical diversity. (See e.g., Matter, 1997, J. Med. Chem. 40:1219-1229).

One method of combinatorial chemistry, affinity fingerprinting, has previously been used to test a discrete library of small molecules for binding affinities for a defined panel of proteins. The fingerprints obtained by the screen are used to predict the affinity of the individual library members for other proteins or receptors of interest (in the instant invention, the protein complexes of the present invention and protein components thereof.) The fingerprints are compared with fingerprints obtained from other compounds known to react with the protein of interest to predict whether the library compound might similarly react. For example, rather than testing every ligand in a large library for interaction with a complex or protein component, only those ligands having a fingerprint similar to other compounds known to have that activity could be tested. (See, e.g., Kauvar et al., 1995, Chem. Biol. 2:107-118; Kauvar, 1995, Affinity fingerprinting, Pharmaceutical Manufacturing International. 8:25-28; and Kauvar, Toxic-Chemical Detection by Pattern Recognition in New Frontiers in Agrochemical Immunoassay, Kurtz, Stanker and Skeritt (eds), 1995, AOAC: Washington, D.C., 305-312).

Kay et al. (1993, Gene 128:59-65) disclosed a method of constructing peptide libraries that encode peptides of totally random sequence that are longer than those of any prior conventional libraries. The libraries disclosed in Kay et al. encode totally synthetic random peptides of greater than about 20 amino acids in length. Such libraries can be advantageously screened to identify complex modulators. (See also U.S. Patent No. 5,498,538 dated March 12, 1996; and PCT Publication No. WO 94/18318 dated August 18, 1994).

A comprehensive review of various types of peptide libraries can be found in Gallop et al., 1994, J. Med. Chem. 37:1233-1251.

#### **4.7 PHARMACEUTICAL COMPOSITIONS AND THERAPEUTIC/PROPHYLACTIC ADMINISTRATION**

The invention provides methods of treatment (and prophylaxis) by administration to a subject of an effective amount of a therapeutic of the invention. In a preferred aspect, the therapeutic is substantially purified. The subject is preferably an animal including, but not limited to animals such as cows, pigs, horses, chickens, cats, dogs, etc., and is preferably a mammal, and most preferably human. In a specific embodiment, a non-human mammal is the subject.

Various delivery systems are known and can be used to administer a therapeutic of the invention, e.g., encapsulation in liposomes, microparticles, and microcapsules; use of recombinant cells capable of expressing the therapeutic, use of receptor-mediated endocytosis (e.g., Wu and Wu, 1987, J. Biol. Chem. 262:4429-4432); construction of a therapeutic nucleic acid as part of a retroviral or other vector, etc. Methods of introduction include but are not limited to intradermal, intramuscular, intraperitoneal, intravenous, subcutaneous, intranasal, epidural, and oral routes. The compounds may be administered by any convenient route, for example by infusion, by bolus injection, by absorption through epithelial or mucocutaneous linings (e.g., oral, rectal and intestinal mucosa, etc.), and may be administered together with other biologically active agents. Administration can be systemic or local. In addition, it may be desirable to introduce the pharmaceutical compositions of the invention into the central nervous system by any suitable route, including intraventricular and intrathecal injection; intraventricular injection may be facilitated by an intraventricular catheter, for example, attached to a reservoir,

such as an Ommaya reservoir. Pulmonary administration can also be employed, e.g., by use of an inhaler or nebulizer, and formulation with an aerosolizing agent.

In a specific embodiment, it may be desirable to administer the pharmaceutical compositions of the invention locally to the area in need of treatment. This may be achieved by, for example, and not by way of limitation, local infusion during surgery, topical application, e.g., in conjunction with a wound dressing after surgery, by injection, by means of a catheter, by means of a suppository, or by means of an implant, said implant being of a porous, non-porous, or gelatinous material, including membranes, such as sialastic membranes, or fibers. In one embodiment, administration can be by direct injection at the site (or former site) of a malignant tumor or neoplastic or pre-neoplastic tissue.

In another embodiment, the therapeutic can be delivered in a vesicle, in particular a liposome (Langer, 1990, *Science* 249:1527-1533; Treat et al., 1989, In: *Liposomes in the Therapy of Infectious Disease and Cancer*, Lopez-Berestein and Fidler, eds., Liss, New York, pp. 353-365; Lopez-Berestein, *ibid.*, pp. 317-327; see generally *ibid.*)

In yet another embodiment, the therapeutic can be delivered via a controlled release system. In one embodiment, a pump may be used (Langer, *supra*; Sefton, 1987, *CRC Crit. Ref. Biomed. Eng.* 14:201-240; Buchwald et al., 1980, *Surgery* 88:507-516; Saudek et al., 1989, *N. Engl. J. Med.* 321:574-579). In another embodiment, polymeric materials can be used (*Medical Applications of Controlled Release*, Langer and Wise, eds., CRC Press, Boca Raton, Florida, 1974; *Controlled Drug Bioavailability, Drug Product Design and Performance*, Smolen and Ball, eds., Wiley, New York, 1984; Ranger and Peppas, 1983, *Macromol. Sci. Rev. Macromol. Chem.* 23:61; Levy et al., 1985, *Science* 228:190-192; During et al., 1989, *Ann. Neurol.* 25:351-356; Howard et al., 1989, *J. Neurosurg.* 71:858-863). In yet another embodiment, a controlled release system can be placed in proximity of the therapeutic target, i.e., the brain, thus requiring only a fraction of the systemic dose (e.g., Goodson, 1984, In: *Medical Applications of Controlled Release*, *supra*, Vol. 2, pp. 115-138). Other controlled release systems are discussed in the review by Langer (1990, *Science* 249:1527-1533).

In a specific embodiment where the therapeutic is a nucleic acid encoding a protein therapeutic, the nucleic acid can be administered in vivo to promote expression of its encoded protein, by constructing it as part of an appropriate nucleic acid expression vector and administering it so that it becomes intracellular, e.g., by use of a retroviral vector (U.S. Patent No. 4,980,286), or by direct injection, or by use of microparticle

bombardment (e.g., a gene gun; Biolistic, Dupont), or by coating it with lipids, cell-surface receptors or transfecting agents, or by administering it in linkage to a homeobox-like peptide which is known to enter the nucleus (e.g., Joliot et al., 1991, Proc. Natl. Acad. Sci. USA 88:1864-1868), etc. Alternatively, a nucleic acid therapeutic can be introduced intracellularly and incorporated by homologous recombination within host cell DNA for expression.

The present invention also provides pharmaceutical compositions. Such compositions comprise a therapeutically effective amount of a therapeutic, and a pharmaceutically acceptable carrier. In a specific embodiment, the term "pharmaceutically acceptable" means approved by a regulatory agency of the Federal or a state government or listed in the U.S. Pharmacopeia or other generally recognized pharmacopeia for use in animals, and more particularly, in humans. The term "carrier" refers to a diluent, adjuvant, excipient, or vehicle with which the therapeutic is administered. Such pharmaceutical carriers can be sterile liquids, such as water and oils, including those of petroleum, animal, vegetable or synthetic origin, including but not limited to peanut oil, soybean oil, mineral oil, sesame oil and the like. Water is a preferred carrier when the pharmaceutical composition is administered orally. Saline and aqueous dextrose are preferred carriers when the pharmaceutical composition is administered intravenously. Saline solutions and aqueous dextrose and glycerol solutions are preferably employed as liquid carriers for injectable solutions. Suitable pharmaceutical excipients include starch, glucose, lactose, sucrose, gelatin, malt, rice, flour, chalk, silica gel, sodium stearate, glycerol monostearate, talc, sodium chloride, dried skim milk, glycerol, propylene, glycol, water, ethanol and the like. The composition, if desired, can also contain minor amounts of wetting or emulsifying agents, or pH buffering agents. These compositions can take the form of solutions, suspensions, emulsions, tablets, pills, capsules, powders, sustained-release formulations and the like. The composition can be formulated as a suppository, with traditional binders and carriers such as triglycerides. Oral formulation can include standard carriers such as pharmaceutical grades of mannitol, lactose, starch, magnesium stearate, sodium saccharine, cellulose, magnesium carbonate, etc. Examples of suitable pharmaceutical carriers are described in "Remington's Pharmaceutical Sciences" by E.W. Martin. Such compositions will contain a therapeutically effective amount of the therapeutic, preferably in purified form, together with a suitable amount of carrier so as to provide the form for



proper administration to the patient. The formulation should suit the mode of administration.

In a preferred embodiment, the composition is formulated, in accordance with routine procedures, as a pharmaceutical composition adapted for intravenous administration to human beings. Typically, compositions for intravenous administration are solutions in sterile isotonic aqueous buffer. Where necessary, the composition may also include a solubilizing agent and a local anesthetic such as lidocaine to ease pain at the site of the injection. Generally, the ingredients are supplied either separately or mixed together in unit dosage form, for example, as a dry lyophilized powder or water-free concentrate in a hermetically sealed container such as an ampoule or sachette indicating the quantity of active agent. Where the composition is to be administered by infusion, it can be dispensed with an infusion bottle containing sterile pharmaceutical grade water or saline. Where the composition is administered by injection, an ampoule of sterile water or saline for injection can be provided so that the ingredients may be mixed prior to administration.

The therapeutics of the invention can be formulated as neutral or salt forms. Pharmaceutically acceptable salts include those formed with free carboxyl groups such as those derived from hydrochloric, phosphoric, acetic, oxalic, tartaric acids, etc., those formed with free amine groups such as those derived from isopropylamine, triethylamine, 2-ethylamino ethanol, histidine, procaine, etc., and those derived from sodium, potassium, ammonium, calcium, and ferric hydroxides, etc.

The amount of the therapeutic of the invention which will be effective in the treatment of a particular disorder or condition will depend on the nature of the disorder or condition, and can be determined by standard clinical techniques. In addition, in vitro assays may optionally be employed to help identify optimal dosage ranges. The precise dose to be employed in the formulation will also depend on the route of administration, and the seriousness of the disease or disorder, and should be decided according to the judgment of the practitioner and each patient's circumstances. However, suitable dosage ranges for intravenous administration are generally about 20-500 micrograms of active compound per kilogram body weight. Suitable dosage ranges for intranasal administration are generally about 0.01 pg/kg body weight to 1 mg/kg body weight. Effective doses may be extrapolated from dose-response curves derived from in vitro or animal model test systems.

Suppositories generally contain active ingredient in the range of 0.5% to 10% by weight; oral formulations preferably contain 10% to 95% active ingredient.

The invention also provides a pharmaceutical pack or kit comprising one or more containers filled with one or more of the ingredients of the pharmaceutical compositions of the invention. Optionally associated with such container(s) can be a notice in the form prescribed by a governmental agency regulating the manufacture, use or sale of pharmaceuticals or biological products, which notice reflects approval by the agency of manufacture, use or sale for human administration.

The invention also provides a pharmaceutical pack or kit comprising one or more containers filled with one or more of the ingredients of the pharmaceutical compositions of the invention. For example, the kit can comprise in one or more containers a first protein, or a functionally active fragment or functionally active derivative thereof, which first protein is selected from the group consisting of proteins listed in the fourth column of table 1; and a second protein, or a functionally active fragment or functionally active derivative thereof, which second protein is selected from the group consisting of proteins listed in the fifth column of table 1.

Alternatively, the kit can comprise in one or more containers, all proteins, functionally active fragments or functionally active derivatives thereof of from the group of proteins in the sixth column of table 1.

The kits of the present invention can also contain expression vectors encoding the essential components of the complex machinery, which components after being expressed can be reconstituted in order to form a biologically active complex. Such a kit preferably also contains the required buffers and reagents. Optionally associated with such container(s) can be instructions for use of the kit and/or a notice in the form prescribed by a governmental agency regulating the manufacture, use or sale of pharmaceuticals or biological products, which notice reflects approval by the agency of manufacture, use or sale for human administration.

#### **4.8 ANIMAL MODELS**

The present invention also provides animal models. In one embodiment, animal models for diseases and disorders involving the protein complexes of the present invention are provided. These animal models are well known in the art. These animal models include,

but are not limited to those which are listed in the section 4.6 (*supra*) as exemplary animal models to study any of the complexes provided in the invention. Such animals can be initially produced by promoting homologous recombination or insertional mutagenesis between genes encoding the protein components of the complexes in the chromosome, and exogenous genes encoding the protein components of the complexes that have been rendered biologically inactive or deleted (preferably by insertion of a heterologous sequence, e.g., an antibiotic resistance gene). In a preferred aspect, homologous recombination is carried out by transforming embryo-derived stem (ES) cells with one or more vectors containing one or more insertionally inactivated genes, such that homologous recombination occurs, followed by injecting the transformed ES cells into a blastocyst, and implanting the blastocyst into a foster mother, followed by the birth of the chimeric animal ("knockout animal") in which a gene encoding a component protein from the fourth column of table 1, or a functionally active fragment or functionally active derivative thereof, and a gene encoding a component protein from the fifth column of table 1, or a functionally active fragment or functionally active derivative thereof, has been inactivated or deleted (Capecchi, 1989, *Science* 244:1288-1292).

In another preferred aspect, homologous recombination is carried out by transforming embryo-derived stem (ES) cells with one or more vectors containing one or more insertionally inactivated genes, such that homologous recombination occurs, followed by injecting the transformed ES cells into a blastocyst, and implanting the blastocyst into a foster mother, followed by the birth of the chimeric animal ("knockout animal") in which the genes of all component proteins from the group of proteins listed in the fourth column of table 1 or of all proteins from the group of proteins listed in the fifth column of table 1 have been inactivated or deleted.

The chimeric animal can be bred to produce additional knockout animals. Such animals can be mice, hamsters, sheep, pigs, cattle, etc., and are preferably non-human mammals. In a specific embodiment, a knockout mouse is produced.

Such knockout animals are expected to develop, or be predisposed to developing, diseases or disorders associated with mutations involving the protein complexes of the present invention, and thus, can have use as animal models of such diseases and disorders, e.g., to screen for or test molecules (e.g., potential therapeutics) for such diseases and disorders.

In a different embodiment of the invention, transgenic animals that have incorporated and express (or over-express or mis-express) a functional gene encoding a

protein component of the complex, e.g. by introducing the a gene encoding one or more of the components of the complex under the control of a heterologous promoter (i.e., a promoter that is not the native promoter of the gene) that either over-expresses the protein or proteins, or expresses them in tissues not normally expressing the complexes or proteins, can have use as animal models of diseases and disorders characterized by elevated levels of the protein complexes. Such animals can be used to screen or test molecules for the ability to treat or prevent the diseases and disorders cited supra.

In one embodiment, the present invention provides a recombinant non-human animal in which an endogenous gene encoding a first protein, or a functionally active fragment or functionally active derivative thereof, which first protein is selected from the group of proteins listed in the fourth column of table 1, and an endogenous gene encoding a second protein, or a functionally active fragment or functionally active derivative thereof, which second protein is selected from the group consisting of proteins listed in the fifth column of table 1 has been deleted or inactivated by homologous recombination or insertional mutagenesis of said animal or an ancestor thereof. In addition, the present invention provides a recombinant non-human animal in which the endogenous genes of all proteins, or functionally active fragments or functionally active derivatives thereof of one of the group of proteins listed in the sixth column have been deleted or inactivated by homologous recombination or insertional mutagenesis of said animal or an ancestor thereof:

In another embodiment, the present invention provides a recombinant non-human animal in which an endogenous gene encoding a first protein, or a functionally active fragment or functionally active derivative thereof, which first protein is selected from the group consisting of proteins of the fourth column of table 1, and an endogenous gene encoding a second protein, or a functionally active fragment or functionally active derivative thereof, which second protein is selected from the group consisting of proteins of the fifth column, of table 1 are recombinantly expressed in said animal or an ancestor thereof.

The following series of examples are presented by way of illustration and not by way of limitation on the scope of the invention.

## EXAMPLES

An object of the present invention was to identify protein complexes of the APP processing pathway, component proteins of the said complexes, fragments and derivatives of the component proteins, and antibodies specific to the complexes. The present invention also relates to methods for use of the complexes of the APP processing pathway and their interacting proteins in, inter alia, screening, diagnosis, and therapy, as well as to methods of preparing the complexes.

By applying the process according to the invention said complexes were identified. The components are listed in table 1.

Those complexes are, as called herein, the following complexes:

Aph1a-complex, APP-695SW-complex, APP-C99-complex, Fe65-complex, Nicastrin-complex, Psen-2-complex, Pen2-complex, Tau-complex, X11 $\beta$ -complex

Thus, the invention relates to the following embodiments:

The present invention relates to the Fe65-complex

1. A protein complex selected from complex (I) and comprising
  - (a) at least one first protein selected from the group consisting of:
    - (i) "APLP1" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions,
    - (ii) "APLP2" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions,
    - (iii) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
    - (iv) "APP-C99" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP-C99" encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid or its complement under low stringency conditions,

(v) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,

(vi) "RNB6" (SEQ ID No:21) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RNB6" encoded by a nucleic acid that hybridizes to the "RNB6" nucleic acid or its complement under low stringency conditions, and

(vii) "Transcription factor CP2" (SEQ ID No:23) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Transcription factor CP2" encoded by a nucleic acid that hybridizes to the "Transcription factor CP2" nucleic acid or its complement under low stringency conditions, and

(b) at least one second protein, which second protein is selected from the group consisting of:

(i) "14-3-3 protein epsilon" (SEQ ID No:1) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein epsilon" encoded by a nucleic acid that hybridizes to the "14-3-3 protein epsilon" nucleic acid or its complement under low stringency conditions,

(ii) "14-3-3 protein beta/alpha" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein beta/alpha" encoded by a nucleic acid that hybridizes to the "14-3-3 protein beta/alpha" nucleic acid or its complement under low stringency conditions,

(iii) "14-3-3 protein eta" (SEQ ID No:3) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein eta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein eta" nucleic acid or its complement under low stringency conditions,

(iv) "14-3-3 protein gamma" (SEQ ID No:4) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein gamma" encoded by a nucleic acid that hybridizes to the "14-3-3 protein gamma" nucleic acid or its complement under low stringency conditions,

(v) "14-3-3 protein tau" (SEQ ID No:5) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein tau" encoded by a nucleic acid that hybridizes to the "14-3-3 protein tau" nucleic acid or its complement under low stringency conditions,

- (vi) "14-3-3 protein zeta/delta" (SEQ ID No:6) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein zeta/delta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein zeta/delta" nucleic acid or its complement under low stringency conditions,
- (vii) "ATP-binding cassette, sub-family B, member 7" (SEQ ID No:11) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family B, member 7" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family B, member 7" nucleic acid or its complement under low stringency conditions,
- (viii) "ECP-51" (SEQ ID No:12) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ECP-51" encoded by a nucleic acid that hybridizes to the "ECP-51" nucleic acid or its complement under low stringency conditions,
- (ix) "GAP-associated tyrosine phosphoprotein p62" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GAP-associated tyrosine phosphoprotein p62" encoded by a nucleic acid that hybridizes to the "GAP-associated tyrosine phosphoprotein p62" nucleic acid or its complement under low stringency conditions,
- (x) "IPI00104084.1" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IPI00104084.1" encoded by a nucleic acid that hybridizes to the "IPI00104084.1" nucleic acid or its complement under low stringency conditions,
- (xi) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions,
- (xii) "Krab box protein ensp00000302970" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Krab box protein ensp00000302970" encoded by a nucleic acid that hybridizes to the "Krab box protein ensp00000302970" nucleic acid or its complement under low stringency conditions,
- (xiii) "PDZ domain protein MAGI-3" (SEQ ID No:18) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"PDZ domain protein MAGI-3" encoded by a nucleic acid that hybridizes to the "PDZ domain protein MAGI-3" nucleic acid or its complement under low stringency conditions,

(xiv) "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" nucleic acid or its complement under low stringency conditions,

(xv) "Protein similar to probable mitotic centromere associated kinesin" (SEQ ID No:20) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to probable mitotic centromere associated kinesin" encoded by a nucleic acid that hybridizes to the "Protein similar to probable mitotic centromere associated kinesin" nucleic acid or its complement under low stringency conditions,

(xvi) "SAP-62" (SEQ ID No:22) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SAP-62" encoded by a nucleic acid that hybridizes to the "SAP-62" nucleic acid or its complement under low stringency conditions, and

(xvii) "Zinc finger protein 277" (SEQ ID No:24) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Zinc finger protein 277" encoded by a nucleic acid that hybridizes to the "Zinc finger protein 277" nucleic acid or its complement under low stringency conditions, and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

2. The protein complex according to No. 1 wherein the first protein is the protein Fe65 (SEQ ID NO. 13), or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of 'Fe65' encoded by a nucleic acid that hybridizes to the 'Fe65' under low stringency conditions.



3. The protein complex according to No. 1 selected from complex (I) and comprising the following proteins:

- (i) "14-3-3 protein epsilon" (SEQ ID No:1) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein epsilon" encoded by a nucleic acid that hybridizes to the "14-3-3 protein epsilon" nucleic acid or its complement under low stringency conditions,
- (ii) "14-3-3 protein beta/alpha" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein beta/alpha" encoded by a nucleic acid that hybridizes to the "14-3-3 protein beta/alpha" nucleic acid or its complement under low stringency conditions,
- (iii) "14-3-3 protein eta" (SEQ ID No:3) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein eta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein eta" nucleic acid or its complement under low stringency conditions,
- (iv) "14-3-3 protein gamma" (SEQ ID No:4) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein gamma" encoded by a nucleic acid that hybridizes to the "14-3-3 protein gamma" nucleic acid or its complement under low stringency conditions,
- (v) "14-3-3 protein tau" (SEQ ID No:5) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein tau" encoded by a nucleic acid that hybridizes to the "14-3-3 protein tau" nucleic acid or its complement under low stringency conditions,
- (vi) "14-3-3 protein zeta/delta" (SEQ ID No:6) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein zeta/delta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein zeta/delta" nucleic acid or its complement under low stringency conditions,
- (vii) "APLP1" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions,
- (viii) "APLP2" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions,

- (ix) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
- (x) "APP-C99" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP-C99" encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid or its complement under low stringency conditions,
- (xi) "ATP-binding cassette, sub-family B, member 7" (SEQ ID No:11) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family B, member 7" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family B, member 7" nucleic acid or its complement under low stringency conditions,
- (xii) "ECP-51" (SEQ ID No:12) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ECP-51" encoded by a nucleic acid that hybridizes to the "ECP-51" nucleic acid or its complement under low stringency conditions,
- (xiii) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,
- (xiv) "GAP-associated tyrosine phosphoprotein p62" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GAP-associated tyrosine phosphoprotein p62" encoded by a nucleic acid that hybridizes to the "GAP-associated tyrosine phosphoprotein p62" nucleic acid or its complement under low stringency conditions,
- (xv) "IPI00104084.1" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IPI00104084.1" encoded by a nucleic acid that hybridizes to the "IPI00104084.1" nucleic acid or its complement under low stringency conditions,
- (xvi) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that

hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions,

(xvii) "Krab box protein ensp00000302970" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Krab box protein ensp00000302970" encoded by a nucleic acid that hybridizes to the "Krab box protein ensp00000302970" nucleic acid or its complement under low stringency conditions,

(xviii) "PDZ domain protein MAGI-3" (SEQ ID No:18) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PDZ domain protein MAGI-3" encoded by a nucleic acid that hybridizes to the "PDZ domain protein MAGI-3" nucleic acid or its complement under low stringency conditions,

(xix) "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" nucleic acid or its complement under low stringency conditions,

(xx) "Protein similar to probable mitotic centromere associated kinesin" (SEQ ID No:20) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to probable mitotic centromere associated kinesin" encoded by a nucleic acid that hybridizes to the "Protein similar to probable mitotic centromere associated kinesin" nucleic acid or its complement under low stringency conditions,

(xxi) "RNB6" (SEQ ID No:21) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RNB6" encoded by a nucleic acid that hybridizes to the "RNB6" nucleic acid or its complement under low stringency conditions,

(xxii) "SAP-62" (SEQ ID No:22) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SAP-62" encoded by a nucleic acid that hybridizes to the "SAP-62" nucleic acid or its complement under low stringency conditions,

(xxiii) "Transcription factor CP2" (SEQ ID No:23) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Transcription factor CP2" encoded by a nucleic acid that hybridizes to the "Transcription factor CP2" nucleic acid or its complement under low stringency conditions, and/or

(xxiv) "Zinc finger protein 277" (SEQ ID No:24) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Zinc finger protein 277" encoded by a nucleic acid that hybridizes to the "Zinc finger protein 277" nucleic acid or its complement under low stringency conditions,

and a protein complex selected from complex (II) and comprising the following proteins:

- (i) "14-3-3 protein epsilon" (SEQ ID No:1) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein epsilon" encoded by a nucleic acid that hybridizes to the "14-3-3 protein epsilon" nucleic acid or its complement under low stringency conditions,
- (ii) "14-3-3 protein beta/alpha" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein beta/alpha" encoded by a nucleic acid that hybridizes to the "14-3-3 protein beta/alpha" nucleic acid or its complement under low stringency conditions,
- (iii) "14-3-3 protein eta" (SEQ ID No:3) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein eta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein eta" nucleic acid or its complement under low stringency conditions,
- (iv) "14-3-3 protein gamma" (SEQ ID No:4) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein gamma" encoded by a nucleic acid that hybridizes to the "14-3-3 protein gamma" nucleic acid or its complement under low stringency conditions,
- (v) "14-3-3 protein tau" (SEQ ID No:5) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein tau" encoded by a nucleic acid that hybridizes to the "14-3-3 protein tau" nucleic acid or its complement under low stringency conditions,
- (vi) "14-3-3 protein zeta/delta" (SEQ ID No:6) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein zeta/delta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein zeta/delta" nucleic acid or its complement under low stringency conditions,
- (vii) "APLP1" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions,

- (viii) "APLP2" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions,
- (ix) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
- (x) "APP-C99" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP-C99" encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid or its complement under low stringency conditions,
- (xi) "ATP-binding cassette, sub-family B, member 7" (SEQ ID No:11) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family B, member 7" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family B, member 7" nucleic acid or its complement under low stringency conditions,
- (xii) "ECP-51" (SEQ ID No:12) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ECP-51" encoded by a nucleic acid that hybridizes to the "ECP-51" nucleic acid or its complement under low stringency conditions,
- (xiii) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,
- (xiv) "GAP-associated tyrosine phosphoprotein p62" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GAP-associated tyrosine phosphoprotein p62" encoded by a nucleic acid that hybridizes to the "GAP-associated tyrosine phosphoprotein p62" nucleic acid or its complement under low stringency conditions,
- (xv) "IPI00104084.1" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IPI00104084.1" encoded by a nucleic acid that hybridizes to the "IPI00104084.1" nucleic acid or its complement under low stringency conditions,

(xvi) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions,

(xvii) "Krab box protein ensp00000302970" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Krab box protein ensp00000302970" encoded by a nucleic acid that hybridizes to the "Krab box protein ensp00000302970" nucleic acid or its complement under low stringency conditions,

(xviii) "PDZ domain protein MAGI-3" (SEQ ID No:18) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PDZ domain protein MAGI-3" encoded by a nucleic acid that hybridizes to the "PDZ domain protein MAGI-3" nucleic acid or its complement under low stringency conditions,

(xix) "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" nucleic acid or its complement under low stringency conditions,

(xx) "Protein similar to probable mitotic centromere associated kinesin" (SEQ ID No:20) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to probable mitotic centromere associated kinesin" encoded by a nucleic acid that hybridizes to the "Protein similar to probable mitotic centromere associated kinesin" nucleic acid or its complement under low stringency conditions,

(xxi) "SAP-62" (SEQ ID No:22) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SAP-62" encoded by a nucleic acid that hybridizes to the "SAP-62" nucleic acid or its complement under low stringency conditions, and/or

(xxii) "Zinc finger protein 277" (SEQ ID No:24) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Zinc finger protein 277" encoded by a nucleic acid that hybridizes to the "Zinc finger protein 277" nucleic acid or its complement under low stringency conditions.

4. The protein complex according to No. 1 comprising all but 1 - 16 of the following proteins:

(i) "14-3-3 protein epsilon" (SEQ ID No:1) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein epsilon" encoded by a nucleic acid that hybridizes to the "14-3-3 protein epsilon" nucleic acid or its complement under low stringency conditions,

(ii) "14-3-3 protein beta/alpha" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein beta/alpha" encoded by a nucleic acid that hybridizes to the "14-3-3 protein beta/alpha" nucleic acid or its complement under low stringency conditions,

(iii) "14-3-3 protein eta" (SEQ ID No:3) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein eta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein eta" nucleic acid or its complement under low stringency conditions,

(iv) "14-3-3 protein gamma" (SEQ ID No:4) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein gamma" encoded by a nucleic acid that hybridizes to the "14-3-3 protein gamma" nucleic acid or its complement under low stringency conditions,

(v) "14-3-3 protein tau" (SEQ ID No:5) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein tau" encoded by a nucleic acid that hybridizes to the "14-3-3 protein tau" nucleic acid or its complement under low stringency conditions,

(vi) "14-3-3 protein zeta/delta" (SEQ ID No:6) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein zeta/delta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein zeta/delta" nucleic acid or its complement under low stringency conditions,

(vii) "APLP1" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions,

(viii) "APLP2" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions,

- (ix) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
- (x) "APP-C99" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP-C99" encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid or its complement under low stringency conditions,
- (xi) "ATP-binding cassette, sub-family B, member 7" (SEQ ID No:11) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family B, member 7" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family B, member 7" nucleic acid or its complement under low stringency conditions,
- (xii) "ECP-51" (SEQ ID No:12) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ECP-51" encoded by a nucleic acid that hybridizes to the "ECP-51" nucleic acid or its complement under low stringency conditions,
- (xiii) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,
- (xiv) "GAP-associated tyrosine phosphoprotein p62" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GAP-associated tyrosine phosphoprotein p62" encoded by a nucleic acid that hybridizes to the "GAP-associated tyrosine phosphoprotein p62" nucleic acid or its complement under low stringency conditions,
- (xv) "IPI00104084.1" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IPI00104084.1" encoded by a nucleic acid that hybridizes to the "IPI00104084.1" nucleic acid or its complement under low stringency conditions,
- (xvi) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that



hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions,

(xvii) "Krab box protein ensp00000302970" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Krab box protein ensp00000302970" encoded by a nucleic acid that hybridizes to the "Krab box protein ensp00000302970" nucleic acid or its complement under low stringency conditions,

(xviii) "PDZ domain protein MAGI-3" (SEQ ID No:18) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PDZ domain protein MAGI-3" encoded by a nucleic acid that hybridizes to the "PDZ domain protein MAGI-3" nucleic acid or its complement under low stringency conditions,

(xix) "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" nucleic acid or its complement under low stringency conditions,

(xx) "Protein similar to probable mitotic centromere associated kinesin" (SEQ ID No:20) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to probable mitotic centromere associated kinesin" encoded by a nucleic acid that hybridizes to the "Protein similar to probable mitotic centromere associated kinesin" nucleic acid or its complement under low stringency conditions,

(xxi) "RNB6" (SEQ ID No:21) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RNB6" encoded by a nucleic acid that hybridizes to the "RNB6" nucleic acid or its complement under low stringency conditions,

(xxii) "SAP-62" (SEQ ID No:22) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SAP-62" encoded by a nucleic acid that hybridizes to the "SAP-62" nucleic acid or its complement under low stringency conditions,

(xxiii) "Transcription factor CP2" (SEQ ID No:23) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Transcription factor CP2" encoded by a nucleic acid that hybridizes to the "Transcription factor CP2" nucleic acid or its complement under low stringency conditions,

(xxiv) "Zinc finger protein 277" (SEQ ID No:24) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Zinc finger protein 277" encoded by a nucleic acid that hybridizes to the "Zinc finger protein 277" nucleic acid or its complement under low stringency conditions.

5. The complex of any of No. 1 - 4 comprising a functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein, respectively.

6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.

7. The complex of any of No. 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.

8. The complex of any of No. 1 - 7 that is involved in the transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)).

9. A process for preparing a complex of any of No. 1 - 8 and optionally the components thereof comprising the following steps: expressing a protein (bait) of the complex,

preferably a tagged protein, in a target cell, isolating the protein complex which is attached to the bait protein, and optionally dissociating the protein complex and isolating the individual complex members.

10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.

11. The process according to any of No. 9 - 10 wherein the two tags are separated by a cleavage site for a protease.

12. Component of the Fe65 complex obtainable by a process according to any of No. 9 - 11.

13. Protein of the Fe65 complex selected from

- (i) "IPI00104084.1" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IPI00104084.1" encoded by a nucleic acid that hybridizes to the "IPI00104084.1" nucleic acid or its complement under low stringency conditions,
- (ii) "Krab box protein ensp00000302970" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Krab box protein ensp00000302970" encoded by a nucleic acid that hybridizes to the "Krab box protein ensp00000302970" nucleic acid or its complement under low stringency conditions,
- (iii) "Protein similar to probable mitotic centromere associated kinesin" (SEQ ID No:20) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to probable mitotic centromere associated kinesin" encoded by a nucleic acid that hybridizes to the "Protein similar to probable mitotic centromere associated kinesin" nucleic acid or its complement under low stringency conditions, and
- (iv) "Zinc finger protein 277" (SEQ ID No:24) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Zinc finger protein 277" encoded by a nucleic acid that hybridizes to the "Zinc finger protein 277" nucleic acid or its complement under low stringency conditions, wherein said low

stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

14. Nucleic acid encoding a protein according to No. 13.

15. Construct, preferably a vector construct, comprising (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or

(b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative of at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the second group of proteins according to No. 1 (b).

16. Host cell, containing a vector comprising at least one of the nucleic acid of No. 14 and/or a construct of No. 15 or containing several vectors each comprising at least the nucleic acid sequence encoding at least one of the proteins, or functionally active fragments or functionally active derivatives thereof selected from the first group of proteins according to No. 1 (a) and the proteins, or functionally active fragments or functionally active derivatives thereof selected from the second group of proteins according to No. 1 (b).

17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody which binds to any of the proteins according to No. 13.

18. A kit comprising in one or more container the complex of any of No. 1 - 8 and/or the proteins of No. 13 optionally together with an antibody according to No. 17 and/or further components such as reagents and working instructions.

19. The kit according to No. 18 for processing a substrate of said complex.

20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative disease such as Alzheimer's disease; inflammatory diseases such as chronic inflammatory disorders, rheumatoid arthritis and inflammatory bowel disease; cancer such as prostate cancer and breast cancer and skin cancer .

21. Array, in which at least a complex according to any of No. 1 - 8 and/or at least one protein according to No. 14 and/or at least one antibody according to No. 17 is attached to a solid carrier.

22. A process for processing a physiological substrate of the complex comprising the step of bringing into contact a complex to any of No. 1 - 8 with said substrate, such that said substrate is processed.

23. A pharmaceutical composition comprising the protein complex of any of No. 1 - 8 and/or any of the following the proteins:

- (i) "IPI00104084.1" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IPI00104084.1" encoded by a nucleic acid that hybridizes to the "IPI00104084.1" nucleic acid or its complement under low stringency conditions,
- (ii) "Krab box protein ensp00000302970" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Krab box protein ensp00000302970" encoded by a nucleic acid that hybridizes to the "Krab box protein ensp00000302970" nucleic acid or its complement under low stringency conditions,
- (iii) "Protein similar to probable mitotic centromere associated kinesin" (SEQ ID No:20) or a functionally active derivative thereof, or a functionally active fragment thereof, or a

homolog thereof, or a variant of "Protein similar to probable mitotic centromere associated kinesin" encoded by a nucleic acid that hybridizes to the "Protein similar to probable mitotic centromere associated kinesin" nucleic acid or its complement under low stringency conditions, and/or

(iv) "Zinc finger protein 277" (SEQ ID No:24) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Zinc finger protein 277" encoded by a nucleic acid that hybridizes to the "Zinc finger protein 277" nucleic acid or its complement under low stringency conditions, and a pharmaceutical acceptable carrier.

24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders such as neurodegenerative disease such as Alzheimer's disease; inflammatory diseases such as chronic inflammatory disorders, rheumatoid arthritis and inflammatory bowel disease; cancer such as prostate cancer and breast cancer and skin cancer .

25. A method for screening for a molecule that binds to the complex of anyone of No. 1 - 8 and/or any of the following the proteins:

(i) "IPI00104084.1" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IPI00104084.1" encoded by a nucleic acid that hybridizes to the "IPI00104084.1" nucleic acid or its complement under low stringency conditions,

(ii) "Krab box protein ensp00000302970" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Krab box protein ensp00000302970" encoded by a nucleic acid that hybridizes to the "Krab box protein ensp00000302970" nucleic acid or its complement under low stringency conditions,

(iii) "Protein similar to probable mitotic centromere associated kinesin" (SEQ ID No:20) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to probable mitotic centromere associated kinesin" encoded by a nucleic acid that hybridizes to the "Protein similar to probable mitotic centromere associated kinesin" nucleic acid or its complement under low stringency conditions, and/or

- (iv) "Zinc finger protein 277" (SEQ ID No:24) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Zinc finger protein 277" encoded by a nucleic acid that hybridizes to the "Zinc finger protein 277" nucleic acid or its complement under low stringency conditions, comprising the steps of
- (a) exposing said complex, or a cell or organism containing same to one or more candidate molecules; and
  - (b) determining whether said candidate molecule is bound to the complex or protein.

26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 - 8 comprising the steps of (a) exposing said complex, or a cell or organism containing Fe65 complex to one or more candidate molecules; and

(b) determining the amount of activity of protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.

27. The method of No. 26, wherein the amount of said complex is determined.

28. The method of No. 26, wherein the activity of said complex is determined.

29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining the processing of said substrate is modified in the presence of said candidate molecule.

30. The method of No. 26, wherein the amount of the individual protein components of said complex are determined.

31. The method of No. 30, wherein said determining step comprises determining whether

- (i) "14-3-3 protein epsilon" (SEQ ID No:1) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein epsilon" encoded by a nucleic acid that hybridizes to the "14-3-3 protein epsilon" nucleic acid or its complement under low stringency conditions, and/or
- (ii) "14-3-3 protein beta/alpha" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein beta/alpha" encoded by a nucleic acid that hybridizes to the "14-3-3 protein beta/alpha" nucleic acid or its complement under low stringency conditions, and/or
- (iii) "14-3-3 protein eta" (SEQ ID No:3) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein eta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein eta" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "14-3-3 protein gamma" (SEQ ID No:4) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein gamma" encoded by a nucleic acid that hybridizes to the "14-3-3 protein gamma" nucleic acid or its complement under low stringency conditions, and/or
- (v) "14-3-3 protein tau" (SEQ ID No:5) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein tau" encoded by a nucleic acid that hybridizes to the "14-3-3 protein tau" nucleic acid or its complement under low stringency conditions, and/or
- (vi) "14-3-3 protein zeta/delta" (SEQ ID No:6) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein zeta/delta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein zeta/delta" nucleic acid or its complement under low stringency conditions, and/or
- (vii) "APLP1" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions, and/or



- (viii) "APLP2" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions, and/or
- (x) "APP-C99" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP-C99" encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "ATP-binding cassette, sub-family B, member 7" (SEQ ID No:11) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family B, member 7" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family B, member 7" nucleic acid or its complement under low stringency conditions, and/or
- (xii) "ECP-51" (SEQ ID No:12) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ECP-51" encoded by a nucleic acid that hybridizes to the "ECP-51" nucleic acid or its complement under low stringency conditions, and/or
- (xiii) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions, and/or
- (xiv) "GAP-associated tyrosine phosphoprotein p62" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GAP-associated tyrosine phosphoprotein p62" encoded by a nucleic acid that hybridizes to the "GAP-associated tyrosine phosphoprotein p62" nucleic acid or its complement under low stringency conditions, and/or
- (xv) "IPI00104084.1" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IPI00104084.1" encoded by a nucleic acid that hybridizes to the "IPI00104084.1" nucleic acid or its complement under low stringency conditions, and/or

- (xvi) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions, and/or
- (xvii) "Krab box protein ensp00000302970" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Krab box protein ensp00000302970" encoded by a nucleic acid that hybridizes to the "Krab box protein ensp00000302970" nucleic acid or its complement under low stringency conditions, and/or
- (xviii) "PDZ domain protein MAGI-3" (SEQ ID No:18) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PDZ domain protein MAGI-3" encoded by a nucleic acid that hybridizes to the "PDZ domain protein MAGI-3" nucleic acid or its complement under low stringency conditions, and/or
- (xix) "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" nucleic acid or its complement under low stringency conditions, and/or
- (xx) "Protein similar to probable mitotic centromere associated kinesin" (SEQ ID No:20) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to probable mitotic centromere associated kinesin" encoded by a nucleic acid that hybridizes to the "Protein similar to probable mitotic centromere associated kinesin" nucleic acid or its complement under low stringency conditions, and/or
- (xxi) "RNB6" (SEQ ID No:21) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RNB6" encoded by a nucleic acid that hybridizes to the "RNB6" nucleic acid or its complement under low stringency conditions, and/or
- (xxii) "SAP-62" (SEQ ID No:22) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SAP-62" encoded by a nucleic acid that hybridizes to the "SAP-62" nucleic acid or its complement under low stringency conditions, and/or

(xxiii) "Transcription factor CP2" (SEQ ID No:23) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Transcription factor CP2" encoded by a nucleic acid that hybridizes to the "Transcription factor CP2" nucleic acid or its complement under low stringency conditions, and/or (xxiv) "Zinc finger protein 277" (SEQ ID No:24) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Zinc finger protein 277" encoded by a nucleic acid that hybridizes to the "Zinc finger protein 277" nucleic acid or its complement under low stringency conditions, is present in the complex.

32. The method of any of No. 26 - 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease; inflammatory diseases such as chronic inflammatory disorders, rheumatoid arthritis and inflammatory bowel disease; cancer such as prostate cancer and breast cancer and skin cancer .

33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 - 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease; inflammatory diseases such as chronic inflammatory disorders, rheumatoid arthritis and inflammatory bowel disease; cancer such as prostate cancer and breast cancer and skin cancer .

34. A method for the production of a pharmaceutical composition comprising carrying out the method of any of No. 1 - 8 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.

35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, activity of, or component composition of, or intracellular localization of the complex of any one of the No. 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the

complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in an analogous sample from a subject not having the disease or disorder or predisposition indicates the presence in the subject of the disease or disorder or predisposition in the subject.

36. The method of No. 35, wherein the amount of said complex is determined.

37. The method of No. 35, wherein the activity of said complex is determined.

38. The method of No. 37, wherein said determining step comprises isolating from the subject said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.

39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.

40. The method of No. 39, wherein said determining step comprises determining whether  
 (i) "14-3-3 protein epsilon" (SEQ ID No:1) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein epsilon" encoded by a nucleic acid that hybridizes to the "14-3-3 protein epsilon" nucleic acid or its complement under low stringency conditions, and/or  
 (ii) "14-3-3 protein beta/alpha" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein beta/alpha" encoded by a nucleic acid that hybridizes to the "14-3-3 protein beta/alpha" nucleic acid or its complement under low stringency conditions, and/or  
 (iii) "14-3-3 protein eta" (SEQ ID No:3) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein eta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein eta" nucleic acid or its complement under low stringency conditions, and/or

- (iv) "14-3-3 protein gamma" (SEQ ID No:4) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein gamma" encoded by a nucleic acid that hybridizes to the "14-3-3 protein gamma" nucleic acid or its complement under low stringency conditions, and/or
- (v) "14-3-3 protein tau" (SEQ ID No:5) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein tau" encoded by a nucleic acid that hybridizes to the "14-3-3 protein tau" nucleic acid or its complement under low stringency conditions, and/or
- (vi) "14-3-3 protein zeta/delta" (SEQ ID No:6) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein zeta/delta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein zeta/delta" nucleic acid or its complement under low stringency conditions, and/or
- (vii) "APLP1" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions, and/or
- (viii) "APLP2" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions, and/or
- (x) "APP-C99" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP-C99" encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "ATP-binding cassette, sub-family B, member 7" (SEQ ID No:11) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family B, member 7" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family B, member 7" nucleic acid or its complement under low stringency conditions, and/or

- (xii) "ECP-51" (SEQ ID No:12) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ECP-51" encoded by a nucleic acid that hybridizes to the "ECP-51" nucleic acid or its complement under low stringency conditions, and/or
- (xiii) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions, and/or
- (xiv) "GAP-associated tyrosine phosphoprotein p62" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GAP-associated tyrosine phosphoprotein p62" encoded by a nucleic acid that hybridizes to the "GAP-associated tyrosine phosphoprotein p62" nucleic acid or its complement under low stringency conditions, and/or
- (xv) "IPI00104084.1" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IPI00104084.1" encoded by a nucleic acid that hybridizes to the "IPI00104084.1" nucleic acid or its complement under low stringency conditions, and/or
- (xvi) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions, and/or
- (xvii) "Krab box protein ensp00000302970" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Krab box protein ensp00000302970" encoded by a nucleic acid that hybridizes to the "Krab box protein ensp00000302970" nucleic acid or its complement under low stringency conditions, and/or
- (xviii) "PDZ domain protein MAGI-3" (SEQ ID No:18) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PDZ domain protein MAGI-3" encoded by a nucleic acid that hybridizes to the "PDZ domain protein MAGI-3" nucleic acid or its complement under low stringency conditions, and/or
- (xix) "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a

homolog thereof, or a variant of "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" nucleic acid or its complement under low stringency conditions, and/or (xx) "Protein similar to probable mitotic centromere associated kinesin" (SEQ ID No:20) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to probable mitotic centromere associated kinesin" encoded by a nucleic acid that hybridizes to the "Protein similar to probable mitotic centromere associated kinesin" nucleic acid or its complement under low stringency conditions, and/or

(xxi) "RNB6" (SEQ ID No:21) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RNB6" encoded by a nucleic acid that hybridizes to the "RNB6" nucleic acid or its complement under low stringency conditions, and/or

(xxii) "SAP-62" (SEQ ID No:22) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SAP-62" encoded by a nucleic acid that hybridizes to the "SAP-62" nucleic acid or its complement under low stringency conditions, and/or

(xxiii) "Transcription factor CP2" (SEQ ID No:23) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Transcription factor CP2" encoded by a nucleic acid that hybridizes to the "Transcription factor CP2" nucleic acid or its complement under low stringency conditions, and/or

(xxiv) "Zinc finger protein 277" (SEQ ID No:24) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Zinc finger protein 277" encoded by a nucleic acid that hybridizes to the "Zinc finger protein 277" nucleic acid or its complement under low stringency conditions, is present in the complex.

41. The complex of any one of No. 1 - 8, or proteins of No. 13 or the antibody or fragment of No. 17, for use in a method of diagnosing a disease or disorder such as neurodegenerative disease such as Alzheimer's disease; inflammatory diseases such as chronic inflammatory disorders, rheumatoid arthritis and inflammatory bowel disease; cancer such as prostate cancer and breast cancer and skin cancer .

42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity or component composition of or intracellular localization of, the complex of anyone of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), or protein components of, said complex.

43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.

44. The method according to No. 42, wherein said disease or disorder involves increased levels of the amount or activity of said complex.

45. Complex of any of No. 1 - 8 and/or protein selected from the following proteins

- (i) "14-3-3 protein epsilon" (SEQ ID No:1) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein epsilon" encoded by a nucleic acid that hybridizes to the "14-3-3 protein epsilon" nucleic acid or its complement under low stringency conditions,
- (ii) "14-3-3 protein beta/alpha" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein beta/alpha" encoded by a nucleic acid that hybridizes to the "14-3-3 protein beta/alpha" nucleic acid or its complement under low stringency conditions,
- (iii) "14-3-3 protein eta" (SEQ ID No:3) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein



eta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein eta" nucleic acid or its complement under low stringency conditions,

(iv) "14-3-3 protein gamma" (SEQ ID No:4) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein gamma" encoded by a nucleic acid that hybridizes to the "14-3-3 protein gamma" nucleic acid or its complement under low stringency conditions,

(v) "14-3-3 protein tau" (SEQ ID No:5) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein tau" encoded by a nucleic acid that hybridizes to the "14-3-3 protein tau" nucleic acid or its complement under low stringency conditions,

(vi) "14-3-3 protein zeta/delta" (SEQ ID No:6) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein zeta/delta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein zeta/delta" nucleic acid or its complement under low stringency conditions,

(vii) "APLP1" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions,

(viii) "APLP2" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions,

(ix) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,

(x) "APP-C99" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP-C99" encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid or its complement under low stringency conditions,

(xi) "ATP-binding cassette, sub-family B, member 7" (SEQ ID No:11) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family B, member 7" encoded by a nucleic

acid that hybridizes to the "ATP-binding cassette, sub-family B, member 7" nucleic acid or its complement under low stringency conditions,

(xii) "ECP-51" (SEQ ID No:12) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ECP-51" encoded by a nucleic acid that hybridizes to the "ECP-51" nucleic acid or its complement under low stringency conditions,

(xiii) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,

(xiv) "GAP-associated tyrosine phosphoprotein p62" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GAP-associated tyrosine phosphoprotein p62" encoded by a nucleic acid that hybridizes to the "GAP-associated tyrosine phosphoprotein p62" nucleic acid or its complement under low stringency conditions,

(xv) "IPI00104084.1" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IPI00104084.1" encoded by a nucleic acid that hybridizes to the "IPI00104084.1" nucleic acid or its complement under low stringency conditions,

(xvi) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions,

(xvii) "Krab box protein ensp00000302970" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Krab box protein ensp00000302970" encoded by a nucleic acid that hybridizes to the "Krab box protein ensp00000302970" nucleic acid or its complement under low stringency conditions,

(xviii) "PDZ domain protein MAGI-3" (SEQ ID No:18) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PDZ domain protein MAGI-3" encoded by a nucleic acid that hybridizes to the "PDZ domain protein MAGI-3" nucleic acid or its complement under low stringency conditions,

- (xix) "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" nucleic acid or its complement under low stringency conditions,
- (xx) "Protein similar to probable mitotic centromere associated kinesin" (SEQ ID No:20) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to probable mitotic centromere associated kinesin" encoded by a nucleic acid that hybridizes to the "Protein similar to probable mitotic centromere associated kinesin" nucleic acid or its complement under low stringency conditions,
- (xxi) "RNB6" (SEQ ID No:21) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RNB6" encoded by a nucleic acid that hybridizes to the "RNB6" nucleic acid or its complement under low stringency conditions,
- (xxii) "SAP-62" (SEQ ID No:22) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SAP-62" encoded by a nucleic acid that hybridizes to the "SAP-62" nucleic acid or its complement under low stringency conditions,
- (xxiii) "Transcription factor CP2" (SEQ ID No:23) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Transcription factor CP2" encoded by a nucleic acid that hybridizes to the "Transcription factor CP2" nucleic acid or its complement under low stringency conditions, and/or (xxiv) "Zinc finger protein 277" (SEQ ID No:24) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Zinc finger protein 277" encoded by a nucleic acid that hybridizes to the "Zinc finger protein 277" nucleic acid or its complement under low stringency conditions, as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease; inflammatory diseases such as chronic inflammatory disorders, rheumatoid arthritis and inflammatory bowel disease; cancer such as prostate cancer and breast cancer and skin cancer.

The invention further relates to the following embodiments of the X11beta-complex:

1. A protein complex selected from complex (I) and comprising
  - (a) at least one first protein selected from the group consisting of:
    - (i) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
    - (ii) "Hunc18a" (SEQ ID No:54) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hunc18a" encoded by a nucleic acid that hybridizes to the "Hunc18a" nucleic acid or its complement under low stringency conditions,
    - (iii) "Neurexin-1" (SEQ ID No:73) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof; or a variant of "Neurexin-1" encoded by a nucleic acid that hybridizes to the "Neurexin-1" nucleic acid or its complement under low stringency conditions,
    - (iv) "SNAP-25" (SEQ ID No:86) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SNAP-25" encoded by a nucleic acid that hybridizes to the "SNAP-25" nucleic acid or its complement under low stringency conditions,
    - (v) "STX1A" (SEQ ID No:88) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STX1A" encoded by a nucleic acid that hybridizes to the "STX1A" nucleic acid or its complement under low stringency conditions, and
    - (vi) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions, and
  - (b) at least one second protein, which second protein is selected from the group consisting of:
    - (i) "ADAMTS-19" (SEQ ID No:25) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ADAMTS-19" encoded by a nucleic acid that hybridizes to the "ADAMTS-19" nucleic acid or its complement under low stringency conditions,

- (ii) "APLP1" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions,
- (iii) "Axonemal dynein heavy chain 8" (SEQ ID No:26) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Axonemal dynein heavy chain 8" encoded by a nucleic acid that hybridizes to the "Axonemal dynein heavy chain 8" nucleic acid or its complement under low stringency conditions,
- (iv) "BAT1" (SEQ ID No:27) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BAT1" encoded by a nucleic acid that hybridizes to the "BAT1" nucleic acid or its complement under low stringency conditions,
- (v) "C20orf11 (sim to a region of RANBPM)" (SEQ ID No:28) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "C20orf11 (sim to a region of RANBPM)" encoded by a nucleic acid that hybridizes to the "C20orf11 (sim to a region of RANBPM)" nucleic acid or its complement under low stringency conditions,
- (vi) "CGB0\_HUMAN" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGB0\_HUMAN" encoded by a nucleic acid that hybridizes to the "CGB0\_HUMAN" nucleic acid or its complement under low stringency conditions,
- (vii) "Cadherin EGF LAG seven-pass G-type receptor 2" (SEQ ID No:30) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2" encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2" nucleic acid or its complement under low stringency conditions,
- (viii) "Calsyntenin-1" (SEQ ID No:31) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-1" encoded by a nucleic acid that hybridizes to the "Calsyntenin-1" nucleic acid or its complement under low stringency conditions,
- (ix) "Calsyntenin-2" (SEQ ID No:32) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-2"

encoded by a nucleic acid that hybridizes to the "Calsyntenin-2" nucleic acid or its complement under low stringency conditions,

(x) "Calsyntenin-3" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-3" encoded by a nucleic acid that hybridizes to the "Calsyntenin-3" nucleic acid or its complement under low stringency conditions,

(xi) "Chondroitin sulfate proteoglycan 6" (SEQ ID No:34) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Chondroitin sulfate proteoglycan 6" encoded by a nucleic acid that hybridizes to the "Chondroitin sulfate proteoglycan 6" nucleic acid or its complement under low stringency conditions,

(xii) "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" (SEQ ID No:35) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" encoded by a nucleic acid that hybridizes to the "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" nucleic acid or its complement under low stringency conditions,

(xiii) "DC6 protein" (SEQ ID No:36) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DC6 protein" encoded by a nucleic acid that hybridizes to the "DC6 protein" nucleic acid or its complement under low stringency conditions,

(xiv) "Dkfzp586c1924" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dkfzp586c1924" encoded by a nucleic acid that hybridizes to the "Dkfzp586c1924" nucleic acid or its complement under low stringency conditions,

(xv) "Dynein light chain 2A " (SEQ ID No:38) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynein light chain 2A " encoded by a nucleic acid that hybridizes to the "Dynein light chain 2A " nucleic acid or its complement under low stringency conditions,

(xvi) "Dynein light chain-A" (SEQ ID No:39) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynein light chain-A" encoded by a nucleic acid that hybridizes to the "Dynein light chain-A" nucleic acid or its complement under low stringency conditions,

(xvii) "ELAVL3" (SEQ ID No:40) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ELAVL3" encoded by a nucleic acid that hybridizes to the "ELAVL3" nucleic acid or its complement under low stringency conditions,

(xviii) "ENG00000168820 (hypothetical protein with p-loop)" (SEQ ID No:41) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENG00000168820 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ENG00000168820 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions,

(xix) "Eukaryotic translation initiation factor 4A, isoform" (SEQ ID No:42) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Eukaryotic translation initiation factor 4A, isoform" encoded by a nucleic acid that hybridizes to the "Eukaryotic translation initiation factor 4A, isoform" nucleic acid or its complement under low stringency conditions,

(xx) "FLJ13910" (SEQ ID No:43) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13910" encoded by a nucleic acid that hybridizes to the "FLJ13910" nucleic acid or its complement under low stringency conditions,

(xxi) "FRAP1" (SEQ ID No:44) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FRAP1" encoded by a nucleic acid that hybridizes to the "FRAP1" nucleic acid or its complement under low stringency conditions,

(xxii) "Filamin, gamma" (SEQ ID No:45) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Filamin, gamma" encoded by a nucleic acid that hybridizes to the "Filamin, gamma" nucleic acid or its complement under low stringency conditions,

(xxiii) "GTP-binding protein ERA" (SEQ ID No:46) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GTP-binding protein ERA" encoded by a nucleic acid that hybridizes to the "GTP-binding protein ERA" nucleic acid or its complement under low stringency conditions,

(xxiv) "HADH2/ERAB (mitochondrial enzyme)" (SEQ ID No:47) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HADH2/ERAB (mitochondrial enzyme)" encoded by a nucleic acid that

hybridizes to the "HADH2/ERAB (mitochondrial enzyme)" nucleic acid or its complement under low stringency conditions,

(xxv) "HDAC2" (SEQ ID No:48) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HDAC2" encoded by a nucleic acid that hybridizes to the "HDAC2" nucleic acid or its complement under low stringency conditions,

(xxvi) "HERC2 protein" (SEQ ID No:49) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HERC2 protein" encoded by a nucleic acid that hybridizes to the "HERC2 protein" nucleic acid or its complement under low stringency conditions,

(xxvii) "HSPC154" (SEQ ID No:50) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC154" encoded by a nucleic acid that hybridizes to the "HSPC154" nucleic acid or its complement under low stringency conditions,

(xxviii) "HSPC245" (SEQ ID No:51) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC245" encoded by a nucleic acid that hybridizes to the "HSPC245" nucleic acid or its complement under low stringency conditions,

(xxix) "HYPOTHETICAL PROTEIN FLJ10618" (SEQ ID No:52) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ10618" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ10618" nucleic acid or its complement under low stringency conditions,

(xxx) "HYPOTHETICAL PROTEIN FLJ12599" (SEQ ID No:53) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ12599" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ12599" nucleic acid or its complement under low stringency conditions,

(xxxi) "Hypothetical protein FLJ10795" (SEQ ID No:55) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ10795" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ10795" nucleic acid or its complement under low stringency conditions,



(xxxii) "Hypothetical protein FLJ20397" (SEQ ID No:56) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ20397" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ20397" nucleic acid or its complement under low stringency conditions,

(xxxiii) "IKAP" (SEQ ID No:57) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IKAP" encoded by a nucleic acid that hybridizes to the "IKAP" nucleic acid or its complement under low stringency conditions,

(xxxiv) "Insulinoma-glucagonoma protein 20" (SEQ ID No:58) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Insulinoma-glucagonoma protein 20" encoded by a nucleic acid that hybridizes to the "Insulinoma-glucagonoma protein 20" nucleic acid or its complement under low stringency conditions,

(xxxv) "KIAA0056" (SEQ ID No:59) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0056" encoded by a nucleic acid that hybridizes to the "KIAA0056" nucleic acid or its complement under low stringency conditions,

(xxxvi) "KIAA0166" (SEQ ID No:60) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0166" encoded by a nucleic acid that hybridizes to the "KIAA0166" nucleic acid or its complement under low stringency conditions,

(xxxvii) "KIAA0325 (FRAGMENT)" (SEQ ID No:61) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0325 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0325 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xxxviii) "KIAA0564" (SEQ ID No:62) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0564" encoded by a nucleic acid that hybridizes to the "KIAA0564" nucleic acid or its complement under low stringency conditions,

(xxxix) "KIAA0763" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions,

(xi) "LIB ( leucine-rich repeat protein)" (SEQ ID No:64) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LIB ( leucine-rich repeat protein)" encoded by a nucleic acid that hybridizes to the "LIB ( leucine-rich repeat protein)" nucleic acid or its complement under low stringency conditions,

(xli) "Laminin, gamma 1 " (SEQ ID No:65) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Laminin, gamma 1 " encoded by a nucleic acid that hybridizes to the "Laminin, gamma 1 " nucleic acid or its complement under low stringency conditions,

(xlii) "MBIP" (SEQ ID No:66) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MBIP" encoded by a nucleic acid that hybridizes to the "MBIP" nucleic acid or its complement under low stringency conditions,

(xliii) "MEGF7 (FRAGMENT)" (SEQ ID No:67) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MEGF7 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "MEGF7 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xliv) "MT-ACT48" (SEQ ID No:68) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MT-ACT48" encoded by a nucleic acid that hybridizes to the "MT-ACT48" nucleic acid or its complement under low stringency conditions,

(xlv) "Myosin IXB" (SEQ ID No:69) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Myosin IXB" encoded by a nucleic acid that hybridizes to the "Myosin IXB" nucleic acid or its complement under low stringency conditions,

(xlii) "NEU1" (SEQ ID No:70) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NEU1" encoded by a nucleic acid that hybridizes to the "NEU1" nucleic acid or its complement under low stringency conditions,

(xlvii) "NIPSNAP1" (SEQ ID No:71) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NIPSNAP1" encoded by a nucleic acid that hybridizes to the "NIPSNAP1" nucleic acid or its complement under low stringency conditions,

(xlviii) "NIPSNAP2" (SEQ ID No:72) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NIPSNAP2" encoded by a nucleic acid that hybridizes to the "NIPSNAP2" nucleic acid or its complement under low stringency conditions,

(xlix) "PDZ and LIM domain protein 1" (SEQ ID No:74) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PDZ and LIM domain protein 1" encoded by a nucleic acid that hybridizes to the "PDZ and LIM domain protein 1" nucleic acid or its complement under low stringency conditions,

(l) "PILB" (SEQ ID No:75) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PILB" encoded by a nucleic acid that hybridizes to the "PILB" nucleic acid or its complement under low stringency conditions,

(li) "PILT" (SEQ ID No:76) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PILT" encoded by a nucleic acid that hybridizes to the "PILT" nucleic acid or its complement under low stringency conditions,

(lii) "Paladin" (SEQ ID No:77) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Paladin" encoded by a nucleic acid that hybridizes to the "Paladin" nucleic acid or its complement under low stringency conditions,

(liii) "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" (SEQ ID No:78) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" encoded by a nucleic acid that hybridizes to the "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" nucleic acid or its complement under low stringency conditions,

(liv) "Procollagen C-endopeptidase enhancer" (SEQ ID No:79) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Procollagen C-endopeptidase enhancer" encoded by a nucleic acid that hybridizes to the "Procollagen C-endopeptidase enhancer" nucleic acid or its complement under low stringency conditions,

(lv) "Programmed cell death 10" (SEQ ID No:80) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Programmed cell death 10" encoded by a nucleic acid that hybridizes to the

"Programmed cell death 10" nucleic acid or its complement under low stringency conditions,

(Ivi) "Protein similar to AGCP6688" (SEQ ID No:81) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to AGCP6688" encoded by a nucleic acid that hybridizes to the "Protein similar to AGCP6688" nucleic acid or its complement under low stringency conditions,

(Ivii) "RAB7L1" (SEQ ID No:82) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB7L1" encoded by a nucleic acid that hybridizes to the "RAB7L1" nucleic acid or its complement under low stringency conditions,

(Iviii) "RANBP1" (SEQ ID No:83) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RANBP1" encoded by a nucleic acid that hybridizes to the "RANBP1" nucleic acid or its complement under low stringency conditions,

(Iix) "RPGR-interacting protein 1" (SEQ ID No:84) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RPGR-interacting protein 1" encoded by a nucleic acid that hybridizes to the "RPGR-interacting protein 1" nucleic acid or its complement under low stringency conditions,

(Ix) "Reelin" (SEQ ID No:85) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Reelin" encoded by a nucleic acid that hybridizes to the "Reelin" nucleic acid or its complement under low stringency conditions,

(Ixi) "STMN3" (SEQ ID No:87) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STMN3" encoded by a nucleic acid that hybridizes to the "STMN3" nucleic acid or its complement under low stringency conditions,

(Ixii) "SUCLA2" (SEQ ID No:89) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SUCLA2" encoded by a nucleic acid that hybridizes to the "SUCLA2" nucleic acid or its complement under low stringency conditions,

(Ixiii) "Serine/threonine protein phosphatase 6" (SEQ ID No:90) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Serine/threonine protein phosphatase 6" encoded by a nucleic acid that

hybridizes to the "Serine/threonine protein phosphatase 6" nucleic acid or its complement under low stringency conditions,

(lxiv) "Sortilin-related receptor " (SEQ ID No:91) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sortilin-related receptor " encoded by a nucleic acid that hybridizes to the "Sortilin-related receptor " nucleic acid or its complement under low stringency conditions,

(lxv) "Synaptogyrin 3" (SEQ ID No:92) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Synaptogyrin 3" encoded by a nucleic acid that hybridizes to the "Synaptogyrin 3" nucleic acid or its complement under low stringency conditions,

(lxvi) "TYK2" (SEQ ID No:93) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TYK2" encoded by a nucleic acid that hybridizes to the "TYK2" nucleic acid or its complement under low stringency conditions,

(lxvii) "Ubiquitin-protein ligase E3-alpha" (SEQ ID No:94) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Ubiquitin-protein ligase E3-alpha" encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase E3-alpha" nucleic acid or its complement under low stringency conditions,

(lxviii) "VGF nerve growth factor inducible protein" (SEQ ID No:95) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "VGF nerve growth factor inducible protein" encoded by a nucleic acid that hybridizes to the "VGF nerve growth factor inducible protein" nucleic acid or its complement under low stringency conditions,

(lxix) "Zinc finger protein 198" (SEQ ID No:97) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Zinc finger protein 198" encoded by a nucleic acid that hybridizes to the "Zinc finger protein 198" nucleic acid or its complement under low stringency conditions,

(lxx) "hypothetical protein MGC13186" (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC13186" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC13186" nucleic acid or its complement under low stringency conditions, and

(lxxi) "similar to SD27354p [*Drosophila melanogaster*] " (SEQ ID No:99) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "similar to SD27354p [*Drosophila melanogaster*] " encoded by a nucleic acid that hybridizes to the "similar to SD27354p [*Drosophila melanogaster*] " nucleic acid or its complement under low stringency conditions, and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

2. The protein complex according to No. 1 wherein the first protein is the protein X11beta (SEQ ID NO. 96), or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of 'X11beta' encoded by a nucleic acid that hybridizes to the 'X11beta' under low stringency conditions.

3. The protein complex according to No. 1 selected from complex (I) and comprising the following proteins:

- (i) "ADAMTS-19" (SEQ ID No:25) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ADAMTS-19" encoded by a nucleic acid that hybridizes to the "ADAMTS-19" nucleic acid or its complement under low stringency conditions,
- (ii) "APLP1" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions,
- (iii) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
- (iv) "Axonemal dynein heavy chain 8" (SEQ ID No:26) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"Axonemal dynein heavy chain 8" encoded by a nucleic acid that hybridizes to the "Axonemal dynein heavy chain 8" nucleic acid or its complement under low stringency conditions,

(v) "BAT1" (SEQ ID No:27) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BAT1" encoded by a nucleic acid that hybridizes to the "BAT1" nucleic acid or its complement under low stringency conditions,

(vi) "C20orf11 (sim to a region of RANBPM)" (SEQ ID No:28) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "C20orf11 (sim to a region of RANBPM)" encoded by a nucleic acid that hybridizes to the "C20orf11 (sim to a region of RANBPM)" nucleic acid or its complement under low stringency conditions,

(vii) "CGB0\_HUMAN" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGB0\_HUMAN" encoded by a nucleic acid that hybridizes to the "CGB0\_HUMAN" nucleic acid or its complement under low stringency conditions,

(viii) "Cadherin EGF LAG seven-pass G-type receptor 2" (SEQ ID No:30) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2" encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2" nucleic acid or its complement under low stringency conditions,

(ix) "Calsyntenin-1" (SEQ ID No:31) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-1" encoded by a nucleic acid that hybridizes to the "Calsyntenin-1" nucleic acid or its complement under low stringency conditions,

(x) "Calsyntenin-2" (SEQ ID No:32) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-2" encoded by a nucleic acid that hybridizes to the "Calsyntenin-2" nucleic acid or its complement under low stringency conditions,

(xi) "Calsyntenin-3" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-3" encoded by a nucleic acid that hybridizes to the "Calsyntenin-3" nucleic acid or its complement under low stringency conditions,

- (xii) "Chondroitin sulfate proteoglycan 6" (SEQ ID No:34) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Chondroitin sulfate proteoglycan 6" encoded by a nucleic acid that hybridizes to the "Chondroitin sulfate proteoglycan 6" nucleic acid or its complement under low stringency conditions,
- (xiii) "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" (SEQ ID No:35) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" encoded by a nucleic acid that hybridizes to the "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" nucleic acid or its complement under low stringency conditions,
- (xiv) "DC6 protein" (SEQ ID No:36) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DC6 protein" encoded by a nucleic acid that hybridizes to the "DC6 protein" nucleic acid or its complement under low stringency conditions,
- (xv) "Dkfzp586c1924" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dkfzp586c1924" encoded by a nucleic acid that hybridizes to the "Dkfzp586c1924" nucleic acid or its complement under low stringency conditions,
- (xvi) "Dynein light chain 2A " (SEQ ID No:38) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynein light chain 2A " encoded by a nucleic acid that hybridizes to the "Dynein light chain 2A " nucleic acid or its complement under low stringency conditions,
- (xvii) "Dynein light chain-A" (SEQ ID No:39) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynein light chain-A" encoded by a nucleic acid that hybridizes to the "Dynein light chain-A" nucleic acid or its complement under low stringency conditions,
- (xviii) "ELAVL3" (SEQ ID No:40) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ELAVL3" encoded by a nucleic acid that hybridizes to the "ELAVL3" nucleic acid or its complement under low stringency conditions,
- (xix) "ENG00000168820 (hypothetical protein with p-loop)" (SEQ ID No:41) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENG00000168820 (hypothetical protein with p-loop)"



encoded by a nucleic acid that hybridizes to the "ENG00000168820 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions,

(xx) "Eukaryotic translation initiation factor 4A, isoform" (SEQ ID No:42) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Eukaryotic translation initiation factor 4A, isoform" encoded by a nucleic acid that hybridizes to the "Eukaryotic translation initiation factor 4A, isoform" nucleic acid or its complement under low stringency conditions,

(xxi) "FLJ13910" (SEQ ID No:43) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13910" encoded by a nucleic acid that hybridizes to the "FLJ13910" nucleic acid or its complement under low stringency conditions,

(xxii) "FRAP1" (SEQ ID No:44) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FRAP1" encoded by a nucleic acid that hybridizes to the "FRAP1" nucleic acid or its complement under low stringency conditions,

(xxiii) "Filamin, gamma" (SEQ ID No:45) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Filamin, gamma" encoded by a nucleic acid that hybridizes to the "Filamin, gamma" nucleic acid or its complement under low stringency conditions,

(xxiv) "GTP-binding protein ERA" (SEQ ID No:46) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GTP-binding protein ERA" encoded by a nucleic acid that hybridizes to the "GTP-binding protein ERA" nucleic acid or its complement under low stringency conditions,

(xxv) "HADH2/ERAB (mitochondrial enzyme)" (SEQ ID No:47) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HADH2/ERAB (mitochondrial enzyme)" encoded by a nucleic acid that hybridizes to the "HADH2/ERAB (mitochondrial enzyme)" nucleic acid or its complement under low stringency conditions,

(xxvi) "HDAC2" (SEQ ID No:48) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HDAC2" encoded by a nucleic acid that hybridizes to the "HDAC2" nucleic acid or its complement under low stringency conditions,

(xxvii) "HERC2 protein" (SEQ ID No:49) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HERC2

protein" encoded by a nucleic acid that hybridizes to the "HERC2 protein" nucleic acid or its complement under low stringency conditions,

(xxviii) "HSPC154" (SEQ ID No:50) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC154" encoded by a nucleic acid that hybridizes to the "HSPC154" nucleic acid or its complement under low stringency conditions,

(xxix) "HSPC245" (SEQ ID No:51) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC245" encoded by a nucleic acid that hybridizes to the "HSPC245" nucleic acid or its complement under low stringency conditions,

(xxx) "HYPOTHETICAL PROTEIN FLJ10618" (SEQ ID No:52) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ10618" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ10618" nucleic acid or its complement under low stringency conditions,

(xxxi) "HYPOTHETICAL PROTEIN FLJ12599" (SEQ ID No:53) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ12599" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ12599" nucleic acid or its complement under low stringency conditions,

(xxxii) "Hunc18a" (SEQ ID No:54) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hunc18a" encoded by a nucleic acid that hybridizes to the "Hunc18a" nucleic acid or its complement under low stringency conditions,

(xxxiii) "Hypothetical protein FLJ10795" (SEQ ID No:55) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ10795" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ10795" nucleic acid or its complement under low stringency conditions,

(xxxiv) "Hypothetical protein FLJ20397" (SEQ ID No:56) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ20397" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ20397" nucleic acid or its complement under low stringency conditions,

(xxxv) "IKAP" (SEQ ID No:57) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IKAP" encoded by a nucleic acid that hybridizes to the "IKAP" nucleic acid or its complement under low stringency conditions,

(xxxvi) "Insulinoma-glucagonoma protein 20" (SEQ ID No:58) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Insulinoma-glucagonoma protein 20" encoded by a nucleic acid that hybridizes to the "Insulinoma-glucagonoma protein 20" nucleic acid or its complement under low stringency conditions,

(xxxvii) "KIAA0056" (SEQ ID No:59) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0056" encoded by a nucleic acid that hybridizes to the "KIAA0056" nucleic acid or its complement under low stringency conditions,

(xxxviii) "KIAA0166" (SEQ ID No:60) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0166" encoded by a nucleic acid that hybridizes to the "KIAA0166" nucleic acid or its complement under low stringency conditions,

(xxxix) "KIAA0325 (FRAGMENT)" (SEQ ID No:61) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0325 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0325 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xl) "KIAA0564" (SEQ ID No:62) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0564" encoded by a nucleic acid that hybridizes to the "KIAA0564" nucleic acid or its complement under low stringency conditions,

(xli) "KIAA0763" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions,

(xlii) "LIB ( leucine-rich repeat protein)" (SEQ ID No:64) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LIB ( leucine-rich repeat protein)" encoded by a nucleic acid that hybridizes to the "LIB ( leucine-rich repeat protein)" nucleic acid or its complement under low stringency conditions,

(xlili) "Laminin, gamma 1 " (SEQ ID No:65) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Laminin, gamma 1 " encoded by a nucleic acid that hybridizes to the "Laminin, gamma 1 " nucleic acid or its complement under low stringency conditions,

(xliv) "MBIP" (SEQ ID No:66) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MBIP" encoded by a nucleic acid that hybridizes to the "MBIP" nucleic acid or its complement under low stringency conditions,

(xlv) "MEGF7 (FRAGMENT)" (SEQ ID No:67) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MEGF7 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "MEGF7 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xlvi) "MT-ACT48" (SEQ ID No:68) or a functionally active derivative thereof; or a functionally active fragment thereof, or a homolog thereof, or a variant of "MT-ACT48" encoded by a nucleic acid that hybridizes to the "MT-ACT48" nucleic acid or its complement under low stringency conditions,

(xlvii) "Myosin IXB" (SEQ ID No:69) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Myosin IXB" encoded by a nucleic acid that hybridizes to the "Myosin IXB" nucleic acid or its complement under low stringency conditions,

(xlviii) "NEU1" (SEQ ID No:70) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NEU1" encoded by a nucleic acid that hybridizes to the "NEU1" nucleic acid or its complement under low stringency conditions,

(xlix) "NIPSNAP1" (SEQ ID No:71) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NIPSNAP1" encoded by a nucleic acid that hybridizes to the "NIPSNAP1" nucleic acid or its complement under low stringency conditions,

(l) "NIPSNAP2" (SEQ ID No:72) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NIPSNAP2" encoded by a nucleic acid that hybridizes to the "NIPSNAP2" nucleic acid or its complement under low stringency conditions,

(li) "Neurexin-1" (SEQ ID No:73) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurexin-1"

encoded by a nucleic acid that hybridizes to the "Neurexin-1" nucleic acid or its complement under low stringency conditions,

(iii) "PDZ and LIM domain protein 1" (SEQ ID No:74) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PDZ and LIM domain protein 1" encoded by a nucleic acid that hybridizes to the "PDZ and LIM domain protein 1" nucleic acid or its complement under low stringency conditions,

(liii) "PILB" (SEQ ID No:75) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PILB" encoded by a nucleic acid that hybridizes to the "PILB" nucleic acid or its complement under low stringency conditions,

(liv) "PILT" (SEQ ID No:76) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PILT" encoded by a nucleic acid that hybridizes to the "PILT" nucleic acid or its complement under low stringency conditions,

(lv) "Paladin" (SEQ ID No:77) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Paladin" encoded by a nucleic acid that hybridizes to the "Paladin" nucleic acid or its complement under low stringency conditions,

(lvi) "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" (SEQ ID No:78) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" encoded by a nucleic acid that hybridizes to the "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" nucleic acid or its complement under low stringency conditions,

(lvii) "Procollagen C-endopeptidase enhancer" (SEQ ID No:79) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Procollagen C-endopeptidase enhancer" encoded by a nucleic acid that hybridizes to the "Procollagen C-endopeptidase enhancer" nucleic acid or its complement under low stringency conditions,

(lviii) "Programmed cell death 10" (SEQ ID No:80) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Programmed cell death 10" encoded by a nucleic acid that hybridizes to the "Programmed cell death 10" nucleic acid or its complement under low stringency conditions,

- (lix) "Protein similar to AGCP6688" (SEQ ID No:81) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to AGCP6688" encoded by a nucleic acid that hybridizes to the "Protein similar to AGCP6688" nucleic acid or its complement under low stringency conditions,
- (lx) "RAB7L1" (SEQ ID No:82) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB7L1" encoded by a nucleic acid that hybridizes to the "RAB7L1" nucleic acid or its complement under low stringency conditions,
- (lxi) "RANBP1" (SEQ ID No:83) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RANBP1" encoded by a nucleic acid that hybridizes to the "RANBP1" nucleic acid or its complement under low stringency conditions,
- (lxii) "RPGR-interacting protein 1" (SEQ ID No:84) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RPGR-interacting protein 1" encoded by a nucleic acid that hybridizes to the "RPGR-interacting protein 1" nucleic acid or its complement under low stringency conditions,
- (lxiii) "Reelin" (SEQ ID No:85) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Reelin" encoded by a nucleic acid that hybridizes to the "Reelin" nucleic acid or its complement under low stringency conditions,
- (lxiv) "SNAP-25" (SEQ ID No:86) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SNAP-25" encoded by a nucleic acid that hybridizes to the "SNAP-25" nucleic acid or its complement under low stringency conditions,
- (lxv) "STMN3" (SEQ ID No:87) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STMN3" encoded by a nucleic acid that hybridizes to the "STMN3" nucleic acid or its complement under low stringency conditions,
- (lxvi) "STX1A" (SEQ ID No:88) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STX1A" encoded by a nucleic acid that hybridizes to the "STX1A" nucleic acid or its complement under low stringency conditions,
- (lxvii) "SUCLA2" (SEQ ID No:89) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SUCLA2"

encoded by a nucleic acid that hybridizes to the "SUCLA2" nucleic acid or its complement under low stringency conditions,

(Ixxviii) "Serine/threonine protein phosphatase 6" (SEQ ID No:90) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Serine/threonine protein phosphatase 6" encoded by a nucleic acid that hybridizes to the "Serine/threonine protein phosphatase 6" nucleic acid or its complement under low stringency conditions,

(Ixxix) "Sortilin-related receptor " (SEQ ID No:91) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sortilin-related receptor " encoded by a nucleic acid that hybridizes to the "Sortilin-related receptor " nucleic acid or its complement under low stringency conditions,

(Ixx) "Synaptogyrin 3" (SEQ ID No:92) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Synaptogyrin 3" encoded by a nucleic acid that hybridizes to the "Synaptogyrin 3" nucleic acid or its complement under low stringency conditions,

(Ixxi) "TYK2" (SEQ ID No:93) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TYK2" encoded by a nucleic acid that hybridizes to the "TYK2" nucleic acid or its complement under low stringency conditions,

(Ixxii) "Ubiquitin-protein ligase E3-alpha" (SEQ ID No:94) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Ubiquitin-protein ligase E3-alpha" encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase E3-alpha" nucleic acid or its complement under low stringency conditions,

(Ixxiii) "VGF nerve growth factor inducible protein" (SEQ ID No:95) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "VGF nerve growth factor inducible protein" encoded by a nucleic acid that hybridizes to the "VGF nerve growth factor inducible protein" nucleic acid or its complement under low stringency conditions,

(Ixxiv) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions,

(lxxv) "Zinc finger protein 198" (SEQ ID No:97) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Zinc finger protein 198" encoded by a nucleic acid that hybridizes to the "Zinc finger protein 198" nucleic acid or its complement under low stringency conditions,

(lxxvi) "hypothetical protein MGC13186" (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC13186" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC13186" nucleic acid or its complement under low stringency conditions, and/or

(lxxvii) "similar to SD27354p [Drosophila melanogaster] " (SEQ ID No:99) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "similar to SD27354p [Drosophila melanogaster] " encoded by a nucleic acid that hybridizes to the "similar to SD27354p [Drosophila melanogaster] " nucleic acid or its complement under low stringency conditions, and a protein complex selected from complex (II) and comprising the following proteins:

(i) "ADAMTS-19" (SEQ ID No:25) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ADAMTS-19" encoded by a nucleic acid that hybridizes to the "ADAMTS-19" nucleic acid or its complement under low stringency conditions,

(ii) "APLP1" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions,

(iii) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,

(iv) "Axonemal dynein heavy chain 8" (SEQ ID No:26) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Axonemal dynein heavy chain 8" encoded by a nucleic acid that hybridizes to the "Axonemal dynein heavy chain 8" nucleic acid or its complement under low stringency conditions,

(v) "BAT1" (SEQ ID No:27) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BAT1" encoded by a



nucleic acid that hybridizes to the "BAT1" nucleic acid or its complement under low stringency conditions,

(vi) "C20orf11 (sim to a region of RANBPM)" (SEQ ID No:28) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "C20orf11 (sim to a region of RANBPM)" encoded by a nucleic acid that hybridizes to the "C20orf11 (sim to a region of RANBPM)" nucleic acid or its complement under low stringency conditions,

(vii) "CGB0\_HUMAN" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGB0\_HUMAN" encoded by a nucleic acid that hybridizes to the "CGB0\_HUMAN" nucleic acid or its complement under low stringency conditions,

(viii) "Cadherin EGF LAG seven-pass G-type receptor 2" (SEQ ID No:30) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2" encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2" nucleic acid or its complement under low stringency conditions,

(ix) "Calsyntenin-1" (SEQ ID No:31) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-1" encoded by a nucleic acid that hybridizes to the "Calsyntenin-1" nucleic acid or its complement under low stringency conditions,

(x) "Calsyntenin-2" (SEQ ID No:32) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-2" encoded by a nucleic acid that hybridizes to the "Calsyntenin-2" nucleic acid or its complement under low stringency conditions,

(xi) "Calsyntenin-3" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-3" encoded by a nucleic acid that hybridizes to the "Calsyntenin-3" nucleic acid or its complement under low stringency conditions,

(xii) "Chondroitin sulfate proteoglycan 6" (SEQ ID No:34) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Chondroitin sulfate proteoglycan 6" encoded by a nucleic acid that hybridizes to the "Chondroitin sulfate proteoglycan 6" nucleic acid or its complement under low stringency conditions,

- (xiii) "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" (SEQ ID No:35) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" encoded by a nucleic acid that hybridizes to the "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" nucleic acid or its complement under low stringency conditions,
- (xiv) "DC6 protein" (SEQ ID No:36) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DC6 protein" encoded by a nucleic acid that hybridizes to the "DC6 protein" nucleic acid or its complement under low stringency conditions,
- (xv) "Dkfzp586c1924" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dkfzp586c1924" encoded by a nucleic acid that hybridizes to the "Dkfzp586c1924" nucleic acid or its complement under low stringency conditions,
- (xvi) "Dynein light chain 2A " (SEQ ID No:38) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynein light chain 2A " encoded by a nucleic acid that hybridizes to the "Dynein light chain 2A " nucleic acid or its complement under low stringency conditions,
- (xvii) "Dynein light chain-A" (SEQ ID No:39) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynein light chain-A" encoded by a nucleic acid that hybridizes to the "Dynein light chain-A" nucleic acid or its complement under low stringency conditions,
- (xviii) "ELAVL3" (SEQ ID No:40) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ELAVL3" encoded by a nucleic acid that hybridizes to the "ELAVL3" nucleic acid or its complement under low stringency conditions,
- (xix) "ENG00000168820 (hypothetical protein with p-loop)" (SEQ ID No:41) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENG00000168820 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ENG00000168820 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions,
- (xx) "Eukaryotic translation initiation factor 4A, isoform" (SEQ ID No:42) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Eukaryotic translation initiation factor 4A, isoform" encoded by a nucleic

acid that hybridizes to the "Eukaryotic translation initiation factor 4A, isoform" nucleic acid or its complement under low stringency conditions,

(xxi) "FLJ13910" (SEQ ID No:43) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13910" encoded by a nucleic acid that hybridizes to the "FLJ13910" nucleic acid or its complement under low stringency conditions,

(xxii) "FRAP1" (SEQ ID No:44) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FRAP1" encoded by a nucleic acid that hybridizes to the "FRAP1" nucleic acid or its complement under low stringency conditions,

(xxiii) "Filamin, gamma" (SEQ ID No:45) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Filamin, gamma" encoded by a nucleic acid that hybridizes to the "Filamin, gamma" nucleic acid or its complement under low stringency conditions,

(xxiv) "GTP-binding protein ERA" (SEQ ID No:46) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GTP-binding protein ERA" encoded by a nucleic acid that hybridizes to the "GTP-binding protein ERA" nucleic acid or its complement under low stringency conditions,

(xxv) "HADH2/ERAB (mitochondrial enzyme)" (SEQ ID No:47) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HADH2/ERAB (mitochondrial enzyme)" encoded by a nucleic acid that hybridizes to the "HADH2/ERAB (mitochondrial enzyme)" nucleic acid or its complement under low stringency conditions,

(xxvi) "HDAC2" (SEQ ID No:48) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HDAC2" encoded by a nucleic acid that hybridizes to the "HDAC2" nucleic acid or its complement under low stringency conditions,

(xxvii) "HERC2 protein" (SEQ ID No:49) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HERC2 protein" encoded by a nucleic acid that hybridizes to the "HERC2 protein" nucleic acid or its complement under low stringency conditions,

(xxviii) "HSPC154" (SEQ ID No:50) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC154"

encoded by a nucleic acid that hybridizes to the "HSPC154" nucleic acid or its complement under low stringency conditions,

(xxix) "HSPC245" (SEQ ID No:51) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC245" encoded by a nucleic acid that hybridizes to the "HSPC245" nucleic acid or its complement under low stringency conditions,

(xxx) "HYPOTHETICAL PROTEIN FLJ10618" (SEQ ID No:52) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ10618" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ10618" nucleic acid or its complement under low stringency conditions,

(xxxi) "HYPOTHETICAL PROTEIN FLJ12599" (SEQ ID No:53) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ12599" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ12599" nucleic acid or its complement under low stringency conditions,

(xxxii) "Hypothetical protein FLJ10795" (SEQ ID No:55) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ10795" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ10795" nucleic acid or its complement under low stringency conditions,

(xxxiii) "Hypothetical protein FLJ20397" (SEQ ID No:56) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ20397" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ20397" nucleic acid or its complement under low stringency conditions,

(xxxiv) "IKAP" (SEQ ID No:57) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IKAP" encoded by a nucleic acid that hybridizes to the "IKAP" nucleic acid or its complement under low stringency conditions,

(xxxv) "Insulinoma-glucagonoma protein 20" (SEQ ID No:58) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Insulinoma-glucagonoma protein 20" encoded by a nucleic acid that

hybridizes to the "Insulinoma-glucagonoma protein 20" nucleic acid or its complement under low stringency conditions,

(xxxvi) "KIAA0056" (SEQ ID No:59) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0056" encoded by a nucleic acid that hybridizes to the "KIAA0056" nucleic acid or its complement under low stringency conditions,

(xxxvii) "KIAA0166" (SEQ ID No:60) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0166" encoded by a nucleic acid that hybridizes to the "KIAA0166" nucleic acid or its complement under low stringency conditions,

(xxxviii) "KIAA0325 (FRAGMENT)" (SEQ ID No:61) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0325 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0325 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xxxix) "KIAA0564" (SEQ ID No:62) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0564" encoded by a nucleic acid that hybridizes to the "KIAA0564" nucleic acid or its complement under low stringency conditions,

(xl) "KIAA0763" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions,

(xli) "LIB ( leucine-rich repeat protein)" (SEQ ID No:64) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LIB ( leucine-rich repeat protein)" encoded by a nucleic acid that hybridizes to the "LIB ( leucine-rich repeat protein)" nucleic acid or its complement under low stringency conditions,

(xlii) "Laminin, gamma 1 " (SEQ ID No:65) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Laminin, gamma 1 " encoded by a nucleic acid that hybridizes to the "Laminin, gamma 1 " nucleic acid or its complement under low stringency conditions,

(xliii) "MBIP" (SEQ ID No:66) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MBIP" encoded by a

nucleic acid that hybridizes to the "MBIP" nucleic acid or its complement under low stringency conditions,

(xlv) "MEGF7 (FRAGMENT)" (SEQ ID No:67) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MEGF7 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "MEGF7 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xlv) "MT-ACT48" (SEQ ID No:68) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MT-ACT48" encoded by a nucleic acid that hybridizes to the "MT-ACT48" nucleic acid or its complement under low stringency conditions,

(xlv) "Myosin IXB" (SEQ ID No:69) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Myosin IXB" encoded by a nucleic acid that hybridizes to the "Myosin IXB" nucleic acid or its complement under low stringency conditions,

(xlvii) "NEU1" (SEQ ID No:70) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NEU1" encoded by a nucleic acid that hybridizes to the "NEU1" nucleic acid or its complement under low stringency conditions,

(xlviii) "NIPSNAP1" (SEQ ID No:71) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NIPSNAP1" encoded by a nucleic acid that hybridizes to the "NIPSNAP1" nucleic acid or its complement under low stringency conditions,

(xlix) "NIPSNAP2" (SEQ ID No:72) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NIPSNAP2" encoded by a nucleic acid that hybridizes to the "NIPSNAP2" nucleic acid or its complement under low stringency conditions,

(I) "PDZ and LIM domain protein 1" (SEQ ID No:74) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PDZ and LIM domain protein 1" encoded by a nucleic acid that hybridizes to the "PDZ and LIM domain protein 1" nucleic acid or its complement under low stringency conditions,

(II) "PILB" (SEQ ID No:75) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PILB" encoded by a

nucleic acid that hybridizes to the "PILB" nucleic acid or its complement under low stringency conditions,

(lii) "PILT" (SEQ ID No:76) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PILT" encoded by a nucleic acid that hybridizes to the "PILT" nucleic acid or its complement under low stringency conditions,

(liii) "Paladin" (SEQ ID No:77) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Paladin" encoded by a nucleic acid that hybridizes to the "Paladin" nucleic acid or its complement under low stringency conditions,

(liv) "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" (SEQ ID No:78) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" encoded by a nucleic acid that hybridizes to the "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" nucleic acid or its complement under low stringency conditions,

(lv) "Procollagen C-endopeptidase enhancer" (SEQ ID No:79) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Procollagen C-endopeptidase enhancer" encoded by a nucleic acid that hybridizes to the "Procollagen C-endopeptidase enhancer" nucleic acid or its complement under low stringency conditions,

(lvi) "Programmed cell death 10" (SEQ ID No:80) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Programmed cell death 10" encoded by a nucleic acid that hybridizes to the "Programmed cell death 10" nucleic acid or its complement under low stringency conditions,

(lvii) "Protein similar to AGCP6688" (SEQ ID No:81) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to AGCP6688" encoded by a nucleic acid that hybridizes to the "Protein similar to AGCP6688" nucleic acid or its complement under low stringency conditions,

(lviii) "RAB7L1" (SEQ ID No:82) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB7L1" encoded by a nucleic acid that hybridizes to the "RAB7L1" nucleic acid or its complement under low stringency conditions,

(lix) "RANBP1" (SEQ ID No:83) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RANBP1" encoded by a nucleic acid that hybridizes to the "RANBP1" nucleic acid or its complement under low stringency conditions,

(lx) "RPGR-interacting protein 1" (SEQ ID No:84) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RPGR-interacting protein 1" encoded by a nucleic acid that hybridizes to the "RPGR-interacting protein 1" nucleic acid or its complement under low stringency conditions,

(lxi) "Reelin" (SEQ ID No:85) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Reelin" encoded by a nucleic acid that hybridizes to the "Reelin" nucleic acid or its complement under low stringency conditions,

(lxii) "STMN3" (SEQ ID No:87) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STMN3" encoded by a nucleic acid that hybridizes to the "STMN3" nucleic acid or its complement under low stringency conditions,

(lxiii) "SUCLA2" (SEQ ID No:89) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SUCLA2" encoded by a nucleic acid that hybridizes to the "SUCLA2" nucleic acid or its complement under low stringency conditions,

(lxiv) "Serine/threonine protein phosphatase 6" (SEQ ID No:90) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Serine/threonine protein phosphatase 6" encoded by a nucleic acid that hybridizes to the "Serine/threonine protein phosphatase 6" nucleic acid or its complement under low stringency conditions,

(lxv) "Sortilin-related receptor " (SEQ ID No:91) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sortilin-related receptor " encoded by a nucleic acid that hybridizes to the "Sortilin-related receptor " nucleic acid or its complement under low stringency conditions,

(lxvi) "Synaptogyrin 3" (SEQ ID No:92) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Synaptogyrin 3" encoded by a nucleic acid that hybridizes to the "Synaptogyrin 3" nucleic acid or its complement under low stringency conditions,



(Ixxvii) "TYK2" (SEQ ID No:93) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TYK2" encoded by a nucleic acid that hybridizes to the "TYK2" nucleic acid or its complement under low stringency conditions,

(Ixxviii) "Ubiquitin-protein ligase E3-alpha" (SEQ ID No:94) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Ubiquitin-protein ligase E3-alpha" encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase E3-alpha" nucleic acid or its complement under low stringency conditions,

(Ixxix) "VGF nerve growth factor inducible protein" (SEQ ID No:95) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "VGF nerve growth factor inducible protein" encoded by a nucleic acid that hybridizes to the "VGF nerve growth factor inducible protein" nucleic acid or its complement under low stringency conditions,

(Ixxx) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions,

(Ixxxi) "Zinc finger protein 198" (SEQ ID No:97) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Zinc finger protein 198" encoded by a nucleic acid that hybridizes to the "Zinc finger protein 198" nucleic acid or its complement under low stringency conditions,

(Ixxxii) "hypothetical protein MGC13186" (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC13186" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC13186" nucleic acid or its complement under low stringency conditions, and/or

(Ixxxiii) "similar to SD27354p [Drosophila melanogaster] " (SEQ ID No:99) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "similar to SD27354p [Drosophila melanogaster] " encoded by a nucleic acid that hybridizes to the "similar to SD27354p [Drosophila melanogaster] " nucleic acid or its complement under low stringency conditions.

4. The protein complex according to No. 1 comprising all but 1 - 70 of the following proteins:

- (i) "ADAMTS-19" (SEQ ID No:25) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ADAMTS-19" encoded by a nucleic acid that hybridizes to the "ADAMTS-19" nucleic acid or its complement under low stringency conditions,
- (ii) "APLP1" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions,
- (iii) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
- (iv) "Axonemal dynein heavy chain 8" (SEQ ID No:26) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Axonemal dynein heavy chain 8" encoded by a nucleic acid that hybridizes to the "Axonemal dynein heavy chain 8" nucleic acid or its complement under low stringency conditions,
- (v) "BAT1" (SEQ ID No:27) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BAT1" encoded by a nucleic acid that hybridizes to the "BAT1" nucleic acid or its complement under low stringency conditions,
- (vi) "C20orf11 (sim to a region of RANBPM)" (SEQ ID No:28) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "C20orf11 (sim to a region of RANBPM)" encoded by a nucleic acid that hybridizes to the "C20orf11 (sim to a region of RANBPM)" nucleic acid or its complement under low stringency conditions,
- (vii) "CGB0\_HUMAN" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGB0\_HUMAN" encoded by a nucleic acid that hybridizes to the "CGB0\_HUMAN" nucleic acid or its complement under low stringency conditions,
- (viii) "Cadherin EGF LAG seven-pass G-type receptor 2" (SEQ ID No:30) or a functionally active derivative thereof, or a functionally active fragment thereof, or a

homolog thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2" encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2" nucleic acid or its complement under low stringency conditions,

(ix) "Calsyntenin-1" (SEQ ID No:31) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-1" encoded by a nucleic acid that hybridizes to the "Calsyntenin-1" nucleic acid or its complement under low stringency conditions,

(x) "Calsyntenin-2" (SEQ ID No:32) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-2" encoded by a nucleic acid that hybridizes to the "Calsyntenin-2" nucleic acid or its complement under low stringency conditions,

(xi) "Calsyntenin-3" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-3" encoded by a nucleic acid that hybridizes to the "Calsyntenin-3" nucleic acid or its complement under low stringency conditions,

(xii) "Chondroitin sulfate proteoglycan 6" (SEQ ID No:34) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Chondroitin sulfate proteoglycan 6" encoded by a nucleic acid that hybridizes to the "Chondroitin sulfate proteoglycan 6" nucleic acid or its complement under low stringency conditions,

(xiii) "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" (SEQ ID No:35) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" encoded by a nucleic acid that hybridizes to the "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" nucleic acid or its complement under low stringency conditions,

(xiv) "DC6 protein" (SEQ ID No:36) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DC6 protein" encoded by a nucleic acid that hybridizes to the "DC6 protein" nucleic acid or its complement under low stringency conditions,

(xv) "Dkfzp586c1924" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dkfzp586c1924" encoded by a nucleic acid that hybridizes to the "Dkfzp586c1924" nucleic acid or its complement under low stringency conditions,

(xvi) "Dynein light chain 2A " (SEQ ID No:38) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynein light chain 2A " encoded by a nucleic acid that hybridizes to the "Dynein light chain 2A " nucleic acid or its complement under low stringency conditions,

(xvii) "Dynein light chain-A" (SEQ ID No:39) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynein light chain-A" encoded by a nucleic acid that hybridizes to the "Dynein light chain-A" nucleic acid or its complement under low stringency conditions,

(xviii) "ELAVL3" (SEQ ID No:40) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ELAVL3" encoded by a nucleic acid that hybridizes to the "ELAVL3" nucleic acid or its complement under low stringency conditions,

(xix) "ENG00000168820 (hypothetical protein with p-loop)" (SEQ ID No:41) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENG00000168820 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ENG00000168820 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions,

(xx) "Eukaryotic translation initiation factor 4A, isoform" (SEQ ID No:42) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Eukaryotic translation initiation factor 4A, isoform" encoded by a nucleic acid that hybridizes to the "Eukaryotic translation initiation factor 4A, isoform" nucleic acid or its complement under low stringency conditions,

(xxi) "FLJ13910" (SEQ ID No:43) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13910" encoded by a nucleic acid that hybridizes to the "FLJ13910" nucleic acid or its complement under low stringency conditions,

(xxii) "FRAP1" (SEQ ID No:44) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FRAP1" encoded by a nucleic acid that hybridizes to the "FRAP1" nucleic acid or its complement under low stringency conditions,

(xxiii) "Filamin, gamma" (SEQ ID No:45) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Filamin, gamma" encoded by a nucleic acid that hybridizes to the "Filamin, gamma" nucleic acid or its complement under low stringency conditions,

- (xxiv) "GTP-binding protein ERA" (SEQ ID No:46) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GTP-binding protein ERA" encoded by a nucleic acid that hybridizes to the "GTP-binding protein ERA" nucleic acid or its complement under low stringency conditions,
- (xxv) "HADH2/ERAB (mitochondrial enzyme)" (SEQ ID No:47) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HADH2/ERAB (mitochondrial enzyme)" encoded by a nucleic acid that hybridizes to the "HADH2/ERAB (mitochondrial enzyme)" nucleic acid or its complement under low stringency conditions,
- (xxvi) "HDAC2" (SEQ ID No:48) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HDAC2" encoded by a nucleic acid that hybridizes to the "HDAC2" nucleic acid or its complement under low stringency conditions,
- (xxvii) "HERC2 protein" (SEQ ID No:49) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HERC2 protein" encoded by a nucleic acid that hybridizes to the "HERC2 protein" nucleic acid or its complement under low stringency conditions,
- (xxviii) "HSPC154" (SEQ ID No:50) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC154" encoded by a nucleic acid that hybridizes to the "HSPC154" nucleic acid or its complement under low stringency conditions,
- (xxix) "HSPC245" (SEQ ID No:51) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC245" encoded by a nucleic acid that hybridizes to the "HSPC245" nucleic acid or its complement under low stringency conditions,
- (xxx) "HYPOTHETICAL PROTEIN FLJ10618" (SEQ ID No:52) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ10618" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ10618" nucleic acid or its complement under low stringency conditions,
- (xxxi) "HYPOTHETICAL PROTEIN FLJ12599" (SEQ ID No:53) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ12599" encoded by a nucleic acid that

hybridizes to the "HYPOTHETICAL PROTEIN FLJ12599" nucleic acid or its complement under low stringency conditions,

(xxxii) "Hunc18a" (SEQ ID No:54) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hunc18a" encoded by a nucleic acid that hybridizes to the "Hunc18a" nucleic acid or its complement under low stringency conditions,

(xxxiii) "Hypothetical protein FLJ10795" (SEQ ID No:55) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ10795" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ10795" nucleic acid or its complement under low stringency conditions,

(xxxiv) "Hypothetical protein FLJ20397" (SEQ ID No:56) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ20397" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ20397" nucleic acid or its complement under low stringency conditions,

(xxxv) "IKAP" (SEQ ID No:57) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IKAP" encoded by a nucleic acid that hybridizes to the "IKAP" nucleic acid or its complement under low stringency conditions,

(xxxvi) "Insulinoma-glucagonoma protein 20" (SEQ ID No:58) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Insulinoma-glucagonoma protein 20" encoded by a nucleic acid that hybridizes to the "Insulinoma-glucagonoma protein 20" nucleic acid or its complement under low stringency conditions,

(xxxvii) "KIAA0056" (SEQ ID No:59) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0056" encoded by a nucleic acid that hybridizes to the "KIAA0056" nucleic acid or its complement under low stringency conditions,

(xxxviii) "KIAA0166" (SEQ ID No:60) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0166" encoded by a nucleic acid that hybridizes to the "KIAA0166" nucleic acid or its complement under low stringency conditions,

(xxxix) "KIAA0325 (FRAGMENT)" (SEQ ID No:61) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0325 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0325 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xli) "KIAA0564" (SEQ ID No:62) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0564" encoded by a nucleic acid that hybridizes to the "KIAA0564" nucleic acid or its complement under low stringency conditions,

(xlii) "KIAA0763" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions,

(xliii) "LIB ( leucine-rich repeat protein)" (SEQ ID No:64) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LIB ( leucine-rich repeat protein)" encoded by a nucleic acid that hybridizes to the "LIB ( leucine-rich repeat protein)" nucleic acid or its complement under low stringency conditions,

(xliv) "Laminin, gamma 1 " (SEQ ID No:65) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Laminin, gamma 1 " encoded by a nucleic acid that hybridizes to the "Laminin, gamma 1 " nucleic acid or its complement under low stringency conditions,

(xlv) "MBIP" (SEQ ID No:66) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MBIP" encoded by a nucleic acid that hybridizes to the "MBIP" nucleic acid or its complement under low stringency conditions,

(xlv) "MEGF7 (FRAGMENT)" (SEQ ID No:67) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MEGF7 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "MEGF7 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xlvii) "MT-ACT48" (SEQ ID No:68) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MT-ACT48" encoded by a nucleic acid that hybridizes to the "MT-ACT48" nucleic acid or its complement under low stringency conditions,

- (xlvii) "Myosin IXB" (SEQ ID No:69) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Myosin IXB" encoded by a nucleic acid that hybridizes to the "Myosin IXB" nucleic acid or its complement under low stringency conditions,
- (xlviii) "NEU1" (SEQ ID No:70) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NEU1" encoded by a nucleic acid that hybridizes to the "NEU1" nucleic acid or its complement under low stringency conditions,
- (xlix) "NIPSNAP1" (SEQ ID No:71) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NIPSNAP1" encoded by a nucleic acid that hybridizes to the "NIPSNAP1" nucleic acid or its complement under low stringency conditions,
- (l) "NIPSNAP2" (SEQ ID No:72) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NIPSNAP2" encoded by a nucleic acid that hybridizes to the "NIPSNAP2" nucleic acid or its complement under low stringency conditions,
- (li) "Neurexin-1" (SEQ ID No:73) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurexin-1" encoded by a nucleic acid that hybridizes to the "Neurexin-1" nucleic acid or its complement under low stringency conditions,
- (lii) "PDZ and LIM domain protein 1" (SEQ ID No:74) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PDZ and LIM domain protein 1" encoded by a nucleic acid that hybridizes to the "PDZ and LIM domain protein 1" nucleic acid or its complement under low stringency conditions,
- (liii) "PILB" (SEQ ID No:75) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PILB" encoded by a nucleic acid that hybridizes to the "PILB" nucleic acid or its complement under low stringency conditions,
- (liv) "PILT" (SEQ ID No:76) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PILT" encoded by a nucleic acid that hybridizes to the "PILT" nucleic acid or its complement under low stringency conditions,



(lv) "Paladin" (SEQ ID No:77) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Paladin" encoded by a nucleic acid that hybridizes to the "Paladin" nucleic acid or its complement under low stringency conditions,

(lvi) "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" (SEQ ID No:78) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" encoded by a nucleic acid that hybridizes to the "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" nucleic acid or its complement under low stringency conditions,

(lvii) "Procollagen C-endopeptidase enhancer" (SEQ ID No:79) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Procollagen C-endopeptidase enhancer" encoded by a nucleic acid that hybridizes to the "Procollagen C-endopeptidase enhancer" nucleic acid or its complement under low stringency conditions,

(lviii) "Programmed cell death 10" (SEQ ID No:80) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Programmed cell death 10" encoded by a nucleic acid that hybridizes to the "Programmed cell death 10" nucleic acid or its complement under low stringency conditions,

(lix) "Protein similar to AGCP6688" (SEQ ID No:81) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to AGCP6688" encoded by a nucleic acid that hybridizes to the "Protein similar to AGCP6688" nucleic acid or its complement under low stringency conditions,

(lx) "RAB7L1" (SEQ ID No:82) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB7L1" encoded by a nucleic acid that hybridizes to the "RAB7L1" nucleic acid or its complement under low stringency conditions,

(lxi) "RANBP1" (SEQ ID No:83) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RANBP1" encoded by a nucleic acid that hybridizes to the "RANBP1" nucleic acid or its complement under low stringency conditions,

(lxii) "RPGR-interacting protein 1" (SEQ ID No:84) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"RPGR-interacting protein 1" encoded by a nucleic acid that hybridizes to the "RPGR-interacting protein 1" nucleic acid or its complement under low stringency conditions,  
 (Ixi) "Reelin" (SEQ ID No:85) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Reelin" encoded by a nucleic acid that hybridizes to the "Reelin" nucleic acid or its complement under low stringency conditions,

(Ixii) "SNAP-25" (SEQ ID No:86) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SNAP-25" encoded by a nucleic acid that hybridizes to the "SNAP-25" nucleic acid or its complement under low stringency conditions,

(Ixiii) "STMN3" (SEQ ID No:87) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STMN3" encoded by a nucleic acid that hybridizes to the "STMN3" nucleic acid or its complement under low stringency conditions,

(Ixiv) "STX1A" (SEQ ID No:88) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STX1A" encoded by a nucleic acid that hybridizes to the "STX1A" nucleic acid or its complement under low stringency conditions,

(Ixv) "SUCLA2" (SEQ ID No:89) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SUCLA2" encoded by a nucleic acid that hybridizes to the "SUCLA2" nucleic acid or its complement under low stringency conditions,

(Ixvi) "Serine/threonine protein phosphatase 6" (SEQ ID No:90) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Serine/threonine protein phosphatase 6" encoded by a nucleic acid that hybridizes to the "Serine/threonine protein phosphatase 6" nucleic acid or its complement under low stringency conditions,

(Ixvii) "Sortilin-related receptor " (SEQ ID No:91) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sortilin-related receptor " encoded by a nucleic acid that hybridizes to the "Sortilin-related receptor " nucleic acid or its complement under low stringency conditions,

(Ixviii) "Synaptogyrin 3" (SEQ ID No:92) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Synaptogyrin

3" encoded by a nucleic acid that hybridizes to the "Synaptogyrin 3" nucleic acid or its complement under low stringency conditions,

(lxxi) "TYK2" (SEQ ID No:93) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TYK2" encoded by a nucleic acid that hybridizes to the "TYK2" nucleic acid or its complement under low stringency conditions,

(lxxii) "Ubiquitin-protein ligase E3-alpha" (SEQ ID No:94) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Ubiquitin-protein ligase E3-alpha" encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase E3-alpha" nucleic acid or its complement under low stringency conditions,

(lxxiii) "VGF nerve growth factor inducible protein" (SEQ ID No:95) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "VGF nerve growth factor inducible protein" encoded by a nucleic acid that hybridizes to the "VGF nerve growth factor inducible protein" nucleic acid or its complement under low stringency conditions,

(lxxiv) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions,

(lxxv) "Zinc finger protein 198" (SEQ ID No:97) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Zinc finger protein 198" encoded by a nucleic acid that hybridizes to the "Zinc finger protein 198" nucleic acid or its complement under low stringency conditions,

(lxxvi) "hypothetical protein MGC13186" (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC13186" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC13186" nucleic acid or its complement under low stringency conditions,

(lxxvii) "similar to SD27354p [Drosophila melanogaster] " (SEQ ID No:99) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "similar to SD27354p [Drosophila melanogaster] " encoded by a nucleic acid that hybridizes to the "similar to SD27354p [Drosophila melanogaster] " nucleic acid or its complement under low stringency conditions.

5. The complex of any of No. 1 - 4 comprising a functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein, respectively.
6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.
7. The complex of any of No. 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.
8. The complex of any of No. 1 - 7 that is involved in the the transactivation of reporter genes by APP-Gal4/VP16 (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)).
9. A process for preparing a complex of any of No. 1 - 8 and optionally the components thereof comprising the following steps: expressing a protein (bait) of the complex, preferably a tagged protein, in a target cell, isolating the protein complex which is attached to the bait protein, and optionally dissociating the protein complex and isolating the individual complex members.

10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.

11. The process according to any of No. 9 - 10 wherein the two tags are separated by a cleavage site for a protease.

12. Component of the X11beta complex obtainable by a process according to any of No. 9 - 11.

13. Protein of the X11beta complex selected from

- (i) "ADAMTS-19" (SEQ ID No:25) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ADAMTS-19" encoded by a nucleic acid that hybridizes to the "ADAMTS-19" nucleic acid or its complement under low stringency conditions,
- (ii) "BAT1" (SEQ ID No:27) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BAT1" encoded by a nucleic acid that hybridizes to the "BAT1" nucleic acid or its complement under low stringency conditions,
- (iii) "C20orf11 (sim to a region of RANBPM)" (SEQ ID No:28) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "C20orf11 (sim to a region of RANBPM)" encoded by a nucleic acid that hybridizes to the "C20orf11 (sim to a region of RANBPM)" nucleic acid or its complement under low stringency conditions,
- (iv) "CGB0\_HUMAN" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGB0\_HUMAN" encoded by a nucleic acid that hybridizes to the "CGB0\_HUMAN" nucleic acid or its complement under low stringency conditions,
- (v) "Cadherin EGF LAG seven-pass G-type receptor 2" (SEQ ID No:30) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2" encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2" nucleic acid or its complement under low stringency conditions,

- (vi) "Calsyntenin-2" (SEQ ID No:32) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-2" encoded by a nucleic acid that hybridizes to the "Calsyntenin-2" nucleic acid or its complement under low stringency conditions,
- (vii) "Calsyntenin-3" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-3" encoded by a nucleic acid that hybridizes to the "Calsyntenin-3" nucleic acid or its complement under low stringency conditions,
- (viii) "Dkfzp586c1924" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dkfzp586c1924" encoded by a nucleic acid that hybridizes to the "Dkfzp586c1924" nucleic acid or its complement under low stringency conditions,
- (ix) "ENG00000168820 (hypothetical protein with p-loop)" (SEQ ID No:41) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENG00000168820 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ENG00000168820 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions,
- (x) "FLJ13910" (SEQ ID No:43) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13910" encoded by a nucleic acid that hybridizes to the "FLJ13910" nucleic acid or its complement under low stringency conditions,
- (xi) "HERC2 protein" (SEQ ID No:49) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HERC2 protein" encoded by a nucleic acid that hybridizes to the "HERC2 protein" nucleic acid or its complement under low stringency conditions,
- (xii) "HSPC154" (SEQ ID No:50) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC154" encoded by a nucleic acid that hybridizes to the "HSPC154" nucleic acid or its complement under low stringency conditions,
- (xiii) "HSPC245" (SEQ ID No:51) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC245" encoded by a nucleic acid that hybridizes to the "HSPC245" nucleic acid or its complement under low stringency conditions,

- (xiv) "HYPOTHETICAL PROTEIN FLJ10618" (SEQ ID No:52) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ10618" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ10618" nucleic acid or its complement under low stringency conditions,
- (xv) "HYPOTHETICAL PROTEIN FLJ12599" (SEQ ID No:53) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ12599" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ12599" nucleic acid or its complement under low stringency conditions,
- (xvi) "Hypothetical protein FLJ20397" (SEQ ID No:56) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ20397" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ20397" nucleic acid or its complement under low stringency conditions,
- (xvii) "KIAA0056" (SEQ ID No:59) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0056" encoded by a nucleic acid that hybridizes to the "KIAA0056" nucleic acid or its complement under low stringency conditions,
- (xviii) "KIAA0166" (SEQ ID No:60) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0166" encoded by a nucleic acid that hybridizes to the "KIAA0166" nucleic acid or its complement under low stringency conditions,
- (xix) "KIAA0564" (SEQ ID No:62) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0564" encoded by a nucleic acid that hybridizes to the "KIAA0564" nucleic acid or its complement under low stringency conditions,
- (xx) "KIAA0763" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions,
- (xxi) "MEGF7 (FRAGMENT)" (SEQ ID No:67) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MEGF7

(FRAGMENT)" encoded by a nucleic acid that hybridizes to the "MEGF7 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xxii) "MT-ACT48" (SEQ ID No:68) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MT-ACT48" encoded by a nucleic acid that hybridizes to the "MT-ACT48" nucleic acid or its complement under low stringency conditions,

(xxiii) "NIPSNAP1" (SEQ ID No:71) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NIPSNAP1" encoded by a nucleic acid that hybridizes to the "NIPSNAP1" nucleic acid or its complement under low stringency conditions,

(xxiv) "PDZ and LIM domain protein 1" (SEQ ID No:74) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PDZ and LIM domain protein 1" encoded by a nucleic acid that hybridizes to the "PDZ and LIM domain protein 1" nucleic acid or its complement under low stringency conditions,

(xxv) "PILB" (SEQ ID No:75) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PILB" encoded by a nucleic acid that hybridizes to the "PILB" nucleic acid or its complement under low stringency conditions,

(xxvi) "PILT" (SEQ ID No:76) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PILT" encoded by a nucleic acid that hybridizes to the "PILT" nucleic acid or its complement under low stringency conditions,

(xxvii) "Paladin" (SEQ ID No:77) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Paladin" encoded by a nucleic acid that hybridizes to the "Paladin" nucleic acid or its complement under low stringency conditions,

(xxviii) "Programmed cell death 10" (SEQ ID No:80) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Programmed cell death 10" encoded by a nucleic acid that hybridizes to the "Programmed cell death 10" nucleic acid or its complement under low stringency conditions,

(xxix) "Protein similar to AGCP6688" (SEQ ID No:81) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of



"Protein similar to AGCP6688" encoded by a nucleic acid that hybridizes to the "Protein similar to AGCP6688" nucleic acid or its complement under low stringency conditions, (xxx) "RAB7L1" (SEQ ID No:82) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB7L1" encoded by a nucleic acid that hybridizes to the "RAB7L1" nucleic acid or its complement under low stringency conditions,

(xxxi) "Ubiquitin-protein ligase E3-alpha" (SEQ ID No:94) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Ubiquitin-protein ligase E3-alpha" encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase E3-alpha" nucleic acid or its complement under low stringency conditions,

(xxxii) "hypothetical protein MGC13186" (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC13186" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC13186" nucleic acid or its complement under low stringency conditions, and

(xxxiii) "similar to SD27354p [*Drosophila melanogaster*] " (SEQ ID No:99) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "similar to SD27354p [*Drosophila melanogaster*] " encoded by a nucleic acid that hybridizes to the "similar to SD27354p [*Drosophila melanogaster*] " nucleic acid or its complement under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

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14. Nucleic acid encoding a protein according to No. 13.

15. Construct, preferably a vector construct, comprising (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or

(b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative of at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the second group of proteins according to No. 1 (b).

16. Host cell, containing a vector comprising at least one of the nucleic acid of No. 14 and/or a construct of No. 15 or containing several vectors each comprising at least the nucleic acid sequence encoding at least one of the proteins, or functionally active fragments or functionally active derivatives thereof selected from the first group of proteins according to No. 1 (a) and the proteins, or functionally active fragments or functionally active derivatives thereof selected from the second group of proteins according to No. 1 (b).

17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody which binds to any of the proteins according to No. 13.

18. A kit comprising in one or more container the complex of any of No. 1 - 8 and/or the proteins of No. 13 optionally together with an antibody according to No. 17 and/or further components such as reagents and working instructions.

19. The kit according to No. 18 for processing a substrate of said complex.

20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative disease such as Alzheimer's disease; inflammatory conditions such as ulcerative colitis, Crohn's disease and atherosclerosis.

21. Array, in which at least a complex according to any of No. 1 - 8 and/or at least one protein according to No. 14 and/or at least one antibody according to No. 17 is attached to a solid carrier.

22. A process for processing a physiological substrate of the complex comprising the step of bringing into contact a complex to any of No. 1 - 8 with said substrate, such that said substrate is processed.

23. A pharmaceutical composition comprising the protein complex of any of No. 1 - 8 and/or any of the following the proteins:

- (i) "ADAMTS-19" (SEQ ID No:25) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ADAMTS-19" encoded by a nucleic acid that hybridizes to the "ADAMTS-19" nucleic acid or its complement under low stringency conditions,
- (ii) "BAT1" (SEQ ID No:27) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BAT1" encoded by a nucleic acid that hybridizes to the "BAT1" nucleic acid or its complement under low stringency conditions,
- (iii) "C20orf11 (sim to a region of RANBPM)" (SEQ ID No:28) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "C20orf11 (sim to a region of RANBPM)" encoded by a nucleic acid that hybridizes to the "C20orf11 (sim to a region of RANBPM)" nucleic acid or its complement under low stringency conditions,
- (iv) "CGB0\_HUMAN" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGB0\_HUMAN" encoded by a nucleic acid that hybridizes to the "CGB0\_HUMAN" nucleic acid or its complement under low stringency conditions,
- (v) "Cadherin EGF LAG seven-pass G-type receptor 2" (SEQ ID No:30) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2" encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2" nucleic acid or its complement under low stringency conditions,
- (vi) "Calsyntenin-2" (SEQ ID No:32) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-2"

encoded by a nucleic acid that hybridizes to the "Calsyntenin-2" nucleic acid or its complement under low stringency conditions,

(vii) "Calsyntenin-3" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-3" encoded by a nucleic acid that hybridizes to the "Calsyntenin-3" nucleic acid or its complement under low stringency conditions,

(viii) "Dkfzp586c1924" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dkfzp586c1924" encoded by a nucleic acid that hybridizes to the "Dkfzp586c1924" nucleic acid or its complement under low stringency conditions,

(ix) "ENG00000168820 (hypothetical protein with p-loop)" (SEQ ID No:41) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENG00000168820 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ENG00000168820 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions,

(x) "FLJ13910" (SEQ ID No:43) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13910" encoded by a nucleic acid that hybridizes to the "FLJ13910" nucleic acid or its complement under low stringency conditions,

(xi) "HERC2 protein" (SEQ ID No:49) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HERC2 protein" encoded by a nucleic acid that hybridizes to the "HERC2 protein" nucleic acid or its complement under low stringency conditions,

(xii) "HSPC154" (SEQ ID No:50) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC154" encoded by a nucleic acid that hybridizes to the "HSPC154" nucleic acid or its complement under low stringency conditions,

(xiii) "HSPC245" (SEQ ID No:51) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC245" encoded by a nucleic acid that hybridizes to the "HSPC245" nucleic acid or its complement under low stringency conditions,

(xiv) "HYPOTHETICAL PROTEIN FLJ10618" (SEQ ID No:52) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ10618" encoded by a nucleic acid that

hybridizes to the "HYPOTHETICAL PROTEIN FLJ10618" nucleic acid or its complement under low stringency conditions,

(xv) "HYPOTHETICAL PROTEIN FLJ12599" (SEQ ID No:53) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ12599" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ12599" nucleic acid or its complement under low stringency conditions,

(xvi) "Hypothetical protein FLJ20397" (SEQ ID No:56) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ20397" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ20397" nucleic acid or its complement under low stringency conditions,

(xvii) "KIAA0056" (SEQ ID No:59) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0056" encoded by a nucleic acid that hybridizes to the "KIAA0056" nucleic acid or its complement under low stringency conditions,

(xviii) "KIAA0166" (SEQ ID No:60) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0166" encoded by a nucleic acid that hybridizes to the "KIAA0166" nucleic acid or its complement under low stringency conditions,

(xix) "KIAA0564" (SEQ ID No:62) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0564" encoded by a nucleic acid that hybridizes to the "KIAA0564" nucleic acid or its complement under low stringency conditions,

(xx) "KIAA0763" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions,

(xxi) "MEGF7 (FRAGMENT)" (SEQ ID No:67) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MEGF7 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "MEGF7 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xxii) "MT-ACT48" (SEQ ID No:68) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MT-ACT48"

encoded by a nucleic acid that hybridizes to the "MT-ACT48" nucleic acid or its complement under low stringency conditions,

(xxiii) "NIPSNAP1" (SEQ ID No:71) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NIPSNAP1" encoded by a nucleic acid that hybridizes to the "NIPSNAP1" nucleic acid or its complement under low stringency conditions,

(xxiv) "PDZ and LIM domain protein 1" (SEQ ID No:74) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PDZ and LIM domain protein 1" encoded by a nucleic acid that hybridizes to the "PDZ and LIM domain protein 1" nucleic acid or its complement under low stringency conditions,

(xxv) "PILB" (SEQ ID No:75) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PILB" encoded by a nucleic acid that hybridizes to the "PILB" nucleic acid or its complement under low stringency conditions,

(xxvi) "PILT" (SEQ ID No:76) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PILT" encoded by a nucleic acid that hybridizes to the "PILT" nucleic acid or its complement under low stringency conditions,

(xxvii) "Paladin" (SEQ ID No:77) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Paladin" encoded by a nucleic acid that hybridizes to the "Paladin" nucleic acid or its complement under low stringency conditions,

(xxviii) "Programmed cell death 10" (SEQ ID No:80) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Programmed cell death 10" encoded by a nucleic acid that hybridizes to the "Programmed cell death 10" nucleic acid or its complement under low stringency conditions,

(xxix) "Protein similar to AGCP6688" (SEQ ID No:81) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to AGCP6688" encoded by a nucleic acid that hybridizes to the "Protein similar to AGCP6688" nucleic acid or its complement under low stringency conditions,

(xxx) "RAB7L1" (SEQ ID No:82) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB7L1"

encoded by a nucleic acid that hybridizes to the "RAB7L1" nucleic acid or its complement under low stringency conditions,

(xxxi) "Ubiquitin-protein ligase E3-alpha" (SEQ ID No:94) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Ubiquitin-protein ligase E3-alpha" encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase E3-alpha" nucleic acid or its complement under low stringency conditions,

(xxxii) "hypothetical protein MGC13186" (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC13186" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC13186" nucleic acid or its complement under low stringency conditions, and/or

(xxxiii) "similar to SD27354p [Drosophila melanogaster] " (SEQ ID No:99) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "similar to SD27354p [Drosophila melanogaster] " encoded by a nucleic acid that hybridizes to the "similar to SD27354p [Drosophila melanogaster] " nucleic acid or its complement under low stringency conditions, and a pharmaceutical acceptable carrier.

24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders such as neurodegenerative disease such as Alzheimer's disease; inflammatory conditions such as ulcerative colitis, Crohn's disease and arteriosclerosis.

25. A method for screening for a molecule that binds to the complex of anyone of No. 1 - 8 and/or any of the following the proteins:

(i) "ADAMTS-19" (SEQ ID No:25) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ADAMTS-19" encoded by a nucleic acid that hybridizes to the "ADAMTS-19" nucleic acid or its complement under low stringency conditions,

(ii) "BAT1" (SEQ ID No:27) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BAT1" encoded by a

nucleic acid that hybridizes to the "BAT1" nucleic acid or its complement under low stringency conditions,

(iii) "C20orf11 (sim to a region of RANBPM)" (SEQ ID No:28) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "C20orf11 (sim to a region of RANBPM)" encoded by a nucleic acid that hybridizes to the "C20orf11 (sim to a region of RANBPM)" nucleic acid or its complement under low stringency conditions,

(iv) "CGB0\_HUMAN" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGB0\_HUMAN" encoded by a nucleic acid that hybridizes to the "CGB0\_HUMAN" nucleic acid or its complement under low stringency conditions,

(v) "Cadherin EGF LAG seven-pass G-type receptor 2" (SEQ ID No:30) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2" encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2" nucleic acid or its complement under low stringency conditions,

(vi) "Calsyntenin-2" (SEQ ID No:32) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-2" encoded by a nucleic acid that hybridizes to the "Calsyntenin-2" nucleic acid or its complement under low stringency conditions,

(vii) "Calsyntenin-3" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-3" encoded by a nucleic acid that hybridizes to the "Calsyntenin-3" nucleic acid or its complement under low stringency conditions,

(viii) "Dkfzp586c1924" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dkfzp586c1924" encoded by a nucleic acid that hybridizes to the "Dkfzp586c1924" nucleic acid or its complement under low stringency conditions,

(ix) "ENG00000168820 (hypothetical protein with p-loop)" (SEQ ID No:41) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENG00000168820 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ENG00000168820 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions,



- (x) "FLJ13910" (SEQ ID No:43) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13910" encoded by a nucleic acid that hybridizes to the "FLJ13910" nucleic acid or its complement under low stringency conditions,
- (xi) "HERC2 protein" (SEQ ID No:49) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HERC2 protein" encoded by a nucleic acid that hybridizes to the "HERC2 protein" nucleic acid or its complement under low stringency conditions,
- (xii) "HSPC154" (SEQ ID No:50) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC154" encoded by a nucleic acid that hybridizes to the "HSPC154" nucleic acid or its complement under low stringency conditions,
- (xiii) "HSPC245" (SEQ ID No:51) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC245" encoded by a nucleic acid that hybridizes to the "HSPC245" nucleic acid or its complement under low stringency conditions,
- (xiv) "HYPOTHETICAL PROTEIN FLJ10618" (SEQ ID No:52) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ10618" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ10618" nucleic acid or its complement under low stringency conditions,
- (xv) "HYPOTHETICAL PROTEIN FLJ12599" (SEQ ID No:53) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ12599" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ12599" nucleic acid or its complement under low stringency conditions,
- (xvi) "Hypothetical protein FLJ20397" (SEQ ID No:56) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ20397" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ20397" nucleic acid or its complement under low stringency conditions,
- (xvii) "KIAA0056" (SEQ ID No:59) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0056"

encoded by a nucleic acid that hybridizes to the "KIAA0056" nucleic acid or its complement under low stringency conditions,

(xviii) "KIAA0166" (SEQ ID No:60) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0166" encoded by a nucleic acid that hybridizes to the "KIAA0166" nucleic acid or its complement under low stringency conditions,

(xix) "KIAA0564" (SEQ ID No:62) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0564" encoded by a nucleic acid that hybridizes to the "KIAA0564" nucleic acid or its complement under low stringency conditions,

(xx) "KIAA0763" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions,

(xxi) "MEGF7 (FRAGMENT)" (SEQ ID No:67) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MEGF7 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "MEGF7 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xxii) "MT-ACT48" (SEQ ID No:68) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MT-ACT48" encoded by a nucleic acid that hybridizes to the "MT-ACT48" nucleic acid or its complement under low stringency conditions,

(xxiii) "NIPSNAP1" (SEQ ID No:71) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NIPSNAP1" encoded by a nucleic acid that hybridizes to the "NIPSNAP1" nucleic acid or its complement under low stringency conditions,

(xxiv) "PDZ and LIM domain protein 1" (SEQ ID No:74) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PDZ and LIM domain protein 1" encoded by a nucleic acid that hybridizes to the "PDZ and LIM domain protein 1" nucleic acid or its complement under low stringency conditions,

(xxv) "PILB" (SEQ ID No:75) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PILB" encoded by a

nucleic acid that hybridizes to the "PILB" nucleic acid or its complement under low stringency conditions,

(xxvi) "PILT" (SEQ ID No:76) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PILT" encoded by a nucleic acid that hybridizes to the "PILT" nucleic acid or its complement under low stringency conditions,

(xxvii) "Paladin" (SEQ ID No:77) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Paladin" encoded by a nucleic acid that hybridizes to the "Paladin" nucleic acid or its complement under low stringency conditions,

(xxviii) "Programmed cell death 10" (SEQ ID No:80) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Programmed cell death 10" encoded by a nucleic acid that hybridizes to the "Programmed cell death 10" nucleic acid or its complement under low stringency conditions,

(xxix) "Protein similar to AGCP6688" (SEQ ID No:81) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to AGCP6688" encoded by a nucleic acid that hybridizes to the "Protein similar to AGCP6688" nucleic acid or its complement under low stringency conditions,

(xxx) "RAB7L1" (SEQ ID No:82) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB7L1" encoded by a nucleic acid that hybridizes to the "RAB7L1" nucleic acid or its complement under low stringency conditions,

(xxxi) "Ubiquitin-protein ligase E3-alpha" (SEQ ID No:94) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Ubiquitin-protein ligase E3-alpha" encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase E3-alpha" nucleic acid or its complement under low stringency conditions,

(xxxii) "hypothetical protein MGC13186" (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC13186" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC13186" nucleic acid or its complement under low stringency conditions, and/or

(xxxiii) "similar to SD27354p [*Drosophila melanogaster*] " (SEQ ID No:99) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "similar to SD27354p [*Drosophila melanogaster*] " encoded by a nucleic acid that hybridizes to the "similar to SD27354p [*Drosophila melanogaster*] " nucleic acid or its complement under low stringency conditions, comprising the steps of

- (a) exposing said complex, or a cell or organism containing same to one or more candidate molecules; and
- (b) determining whether said candidate molecule is bound to the complex or protein.

26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 - 8 comprising the steps of (a) exposing said complex, or a cell or organism containing X11beta complex to one or more candidate molecules; and

(b) determining the amount of activity of protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.

27. The method of No. 26, wherein the amount of said complex is determined.

28. The method of No. 26, wherein the activity of said complex is determined.

29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of

said complex and determining the processing of said substrate is modified in the presence of said candidate molecule.

30. The method of No. 26, wherein the amount of the individual protein components of said complex are determined.

31. The method of No. 30, wherein said determining step comprises determining whether (i) "ADAMTS-19" (SEQ ID No:25) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ADAMTS-19" encoded by a nucleic acid that hybridizes to the "ADAMTS-19" nucleic acid or its complement under low stringency conditions, and/or

(ii) "APLP1" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions, and/or

(iii) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions, and/or

(iv) "Axonemal dynein heavy chain 8" (SEQ ID No:26) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Axonemal dynein heavy chain 8" encoded by a nucleic acid that hybridizes to the "Axonemal dynein heavy chain 8" nucleic acid or its complement under low stringency conditions, and/or

(v) "BAT1" (SEQ ID No:27) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BAT1" encoded by a nucleic acid that hybridizes to the "BAT1" nucleic acid or its complement under low stringency conditions, and/or

(vi) "C20orf11 (sim to a region of RANBPM)" (SEQ ID No:28) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "C20orf11 (sim to a region of RANBPM)" encoded by a nucleic acid that hybridizes to the "C20orf11 (sim to a region of RANBPM)" nucleic acid or its complement under low stringency conditions, and/or

- (vii) "CGB0\_HUMAN" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGB0\_HUMAN" encoded by a nucleic acid that hybridizes to the "CGB0\_HUMAN" nucleic acid or its complement under low stringency conditions, and/or
- (viii) "Cadherin EGF LAG seven-pass G-type receptor 2" (SEQ ID No:30) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2" encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "Calsyntenin-1" (SEQ ID No:31) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-1" encoded by a nucleic acid that hybridizes to the "Calsyntenin-1" nucleic acid or its complement under low stringency conditions, and/or
- (x) "Calsyntenin-2" (SEQ ID No:32) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-2" encoded by a nucleic acid that hybridizes to the "Calsyntenin-2" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "Calsyntenin-3" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-3" encoded by a nucleic acid that hybridizes to the "Calsyntenin-3" nucleic acid or its complement under low stringency conditions, and/or
- (xii) "Chondroitin sulfate proteoglycan 6" (SEQ ID No:34) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Chondroitin sulfate proteoglycan 6" encoded by a nucleic acid that hybridizes to the "Chondroitin sulfate proteoglycan 6" nucleic acid or its complement under low stringency conditions, and/or
- (xiii) "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" (SEQ ID No:35) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" encoded by a nucleic acid that hybridizes to the "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" nucleic acid or its complement under low stringency conditions, and/or
- (xiv) "DC6 protein" (SEQ ID No:36) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DC6 protein"

encoded by a nucleic acid that hybridizes to the "DC6 protein" nucleic acid or its complement under low stringency conditions, and/or

(xv) "Dkfzp586c1924" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"Dkfzp586c1924" encoded by a nucleic acid that hybridizes to the "Dkfzp586c1924" nucleic acid or its complement under low stringency conditions, and/or

(xvi) "Dynein light chain 2A " (SEQ ID No:38) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynein light chain 2A " encoded by a nucleic acid that hybridizes to the "Dynein light chain 2A "

nucleic acid or its complement under low stringency conditions, and/or

(xvii) "Dynein light chain-A" (SEQ ID No:39) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynein light chain-A" encoded by a nucleic acid that hybridizes to the "Dynein light chain-A" nucleic acid or its complement under low stringency conditions, and/or

(xviii) "ELAVL3" (SEQ ID No:40) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ELAVL3" encoded by a nucleic acid that hybridizes to the "ELAVL3" nucleic acid or its complement under low stringency conditions, and/or

(xix) "ENG00000168820 (hypothetical protein with p-loop)" (SEQ ID No:41) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENG00000168820 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ENG00000168820 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions, and/or

(xx) "Eukaryotic translation initiation factor 4A, isoform" (SEQ ID No:42) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Eukaryotic translation initiation factor 4A, isoform" encoded by a nucleic acid that hybridizes to the "Eukaryotic translation initiation factor 4A, isoform" nucleic acid or its complement under low stringency conditions, and/or

(xxi) "FLJ13910" (SEQ ID No:43) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13910" encoded by a nucleic acid that hybridizes to the "FLJ13910" nucleic acid or its complement under low stringency conditions, and/or

(xxii) "FRAP1" (SEQ ID No:44) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FRAP1" encoded by a

nucleic acid that hybridizes to the "FRAP1" nucleic acid or its complement under low stringency conditions, and/or

(xxiii) "Filamin, gamma" (SEQ ID No:45) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Filamin, gamma" encoded by a nucleic acid that hybridizes to the "Filamin, gamma" nucleic acid or its complement under low stringency conditions, and/or

(xxiv) "GTP-binding protein ERA" (SEQ ID No:46) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GTP-binding protein ERA" encoded by a nucleic acid that hybridizes to the "GTP-binding protein ERA" nucleic acid or its complement under low stringency conditions, and/or

(xxv) "HADH2/ERAB (mitochondrial enzyme)" (SEQ ID No:47) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HADH2/ERAB (mitochondrial enzyme)" encoded by a nucleic acid that hybridizes to the "HADH2/ERAB (mitochondrial enzyme)" nucleic acid or its complement under low stringency conditions, and/or

(xxvi) "HDAC2" (SEQ ID No:48) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HDAC2" encoded by a nucleic acid that hybridizes to the "HDAC2" nucleic acid or its complement under low stringency conditions, and/or

(xxvii) "HERC2 protein" (SEQ ID No:49) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HERC2 protein" encoded by a nucleic acid that hybridizes to the "HERC2 protein" nucleic acid or its complement under low stringency conditions, and/or

(xxviii) "HSPC154" (SEQ ID No:50) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC154" encoded by a nucleic acid that hybridizes to the "HSPC154" nucleic acid or its complement under low stringency conditions, and/or

(xxix) "HSPC245" (SEQ ID No:51) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC245" encoded by a nucleic acid that hybridizes to the "HSPC245" nucleic acid or its complement under low stringency conditions, and/or

(xxx) "HYPOTHETICAL PROTEIN FLJ10618" (SEQ ID No:52) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a



variant of "HYPOTHETICAL PROTEIN FLJ10618" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ10618" nucleic acid or its complement under low stringency conditions, and/or

(xxxi) "HYPOTHETICAL PROTEIN FLJ12599" (SEQ ID No:53) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ12599" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ12599" nucleic acid or its complement under low stringency conditions, and/or

(xxxii) "Hunc18a" (SEQ ID No:54) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hunc18a" encoded by a nucleic acid that hybridizes to the "Hunc18a" nucleic acid or its complement under low stringency conditions, and/or

(xxxiii) "Hypothetical protein FLJ10795" (SEQ ID No:55) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ10795" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ10795" nucleic acid or its complement under low stringency conditions, and/or

(xxxiv) "Hypothetical protein FLJ20397" (SEQ ID No:56) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ20397" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ20397" nucleic acid or its complement under low stringency conditions, and/or

(xxxv) "IKAP" (SEQ ID No:57) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IKAP" encoded by a nucleic acid that hybridizes to the "IKAP" nucleic acid or its complement under low stringency conditions, and/or

(xxxvi) "Insulinoma-glucagonoma protein 20" (SEQ ID No:58) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Insulinoma-glucagonoma protein 20" encoded by a nucleic acid that hybridizes to the "Insulinoma-glucagonoma protein 20" nucleic acid or its complement under low stringency conditions, and/or

(xxxvii) "KIAA0056" (SEQ ID No:59) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0056"

encoded by a nucleic acid that hybridizes to the "KIAA0056" nucleic acid or its complement under low stringency conditions, and/or

(xxxviii) "KIAA0166" (SEQ ID No:60) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0166" encoded by a nucleic acid that hybridizes to the "KIAA0166" nucleic acid or its complement under low stringency conditions, and/or

(xxxix) "KIAA0325 (FRAGMENT)" (SEQ ID No:61) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0325 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0325 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or

(xl) "KIAA0564" (SEQ ID No:62) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0564" encoded by a nucleic acid that hybridizes to the "KIAA0564" nucleic acid or its complement under low stringency conditions, and/or

(xli) "KIAA0763" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions, and/or

(xlii) "LIB ( leucine-rich repeat protein)" (SEQ ID No:64) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LIB ( leucine-rich repeat protein)" encoded by a nucleic acid that hybridizes to the "LIB ( leucine-rich repeat protein)" nucleic acid or its complement under low stringency conditions, and/or

(xlili) "Laminin, gamma 1 " (SEQ ID No:65) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Laminin, gamma 1 " encoded by a nucleic acid that hybridizes to the "Laminin, gamma 1 " nucleic acid or its complement under low stringency conditions, and/or

(xliv) "MBIP" (SEQ ID No:66) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MBIP" encoded by a nucleic acid that hybridizes to the "MBIP" nucleic acid or its complement under low stringency conditions, and/or

(xlv) "MEGF7 (FRAGMENT)" (SEQ ID No:67) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MEGF7

(FRAGMENT)" encoded by a nucleic acid that hybridizes to the "MEGF7 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or

(xlvi) "MT-ACT48" (SEQ ID No:68) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MT-ACT48" encoded by a nucleic acid that hybridizes to the "MT-ACT48" nucleic acid or its complement under low stringency conditions, and/or

(xlvii) "Myosin IXB" (SEQ ID No:69) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Myosin IXB" encoded by a nucleic acid that hybridizes to the "Myosin IXB" nucleic acid or its complement under low stringency conditions, and/or

(xlviii) "NEU1" (SEQ ID No:70) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NEU1" encoded by a nucleic acid that hybridizes to the "NEU1" nucleic acid or its complement under low stringency conditions, and/or

(xlix) "NIPSNAP1" (SEQ ID No:71) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NIPSNAP1" encoded by a nucleic acid that hybridizes to the "NIPSNAP1" nucleic acid or its complement under low stringency conditions, and/or

(i) "NIPSNAP2" (SEQ ID No:72) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NIPSNAP2" encoded by a nucleic acid that hybridizes to the "NIPSNAP2" nucleic acid or its complement under low stringency conditions, and/or

(ii) "Neurexin-1" (SEQ ID No:73) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurexin-1" encoded by a nucleic acid that hybridizes to the "Neurexin-1" nucleic acid or its complement under low stringency conditions, and/or

(iii) "PDZ and LIM domain protein 1" (SEQ ID No:74) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PDZ and LIM domain protein 1" encoded by a nucleic acid that hybridizes to the "PDZ and LIM domain protein 1" nucleic acid or its complement under low stringency conditions, and/or

(liii) "PILB" (SEQ ID No:75) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PILB" encoded by a

nucleic acid that hybridizes to the "PILB" nucleic acid or its complement under low stringency conditions, and/or

(liv) "PILT" (SEQ ID No:76) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PILT" encoded by a nucleic acid that hybridizes to the "PILT" nucleic acid or its complement under low stringency conditions, and/or

(lv) "Paladin" (SEQ ID No:77) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Paladin" encoded by a nucleic acid that hybridizes to the "Paladin" nucleic acid or its complement under low stringency conditions, and/or

(lvi) "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" (SEQ ID No:78) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" encoded by a nucleic acid that hybridizes to the "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" nucleic acid or its complement under low stringency conditions, and/or

(lvii) "Procollagen C-endopeptidase enhancer" (SEQ ID No:79) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Procollagen C-endopeptidase enhancer" encoded by a nucleic acid that hybridizes to the "Procollagen C-endopeptidase enhancer" nucleic acid or its complement under low stringency conditions, and/or

(lviii) "Programmed cell death 10" (SEQ ID No:80) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Programmed cell death 10" encoded by a nucleic acid that hybridizes to the "Programmed cell death 10" nucleic acid or its complement under low stringency conditions, and/or

(lix) "Protein similar to AGCP6688" (SEQ ID No:81) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to AGCP6688" encoded by a nucleic acid that hybridizes to the "Protein similar to AGCP6688" nucleic acid or its complement under low stringency conditions, and/or

(lx) "RAB7L1" (SEQ ID No:82) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB7L1" encoded by a nucleic acid that hybridizes to the "RAB7L1" nucleic acid or its complement under low stringency conditions, and/or

(Ixi) "RANBP1" (SEQ ID No:83) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RANBP1" encoded by a nucleic acid that hybridizes to the "RANBP1" nucleic acid or its complement under low stringency conditions, and/or

(Ixii) "RPGR-interacting protein 1" (SEQ ID No:84) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RPGR-interacting protein 1" encoded by a nucleic acid that hybridizes to the "RPGR-interacting protein 1" nucleic acid or its complement under low stringency conditions, and/or

(Ixiii) "Reelin" (SEQ ID No:85) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Reelin" encoded by a nucleic acid that hybridizes to the "Reelin" nucleic acid or its complement under low stringency conditions, and/or

(Ixiv) "SNAP-25" (SEQ ID No:86) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SNAP-25" encoded by a nucleic acid that hybridizes to the "SNAP-25" nucleic acid or its complement under low stringency conditions, and/or

(Ixv) "STMN3" (SEQ ID No:87) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STMN3" encoded by a nucleic acid that hybridizes to the "STMN3" nucleic acid or its complement under low stringency conditions, and/or

(Ixvi) "STX1A" (SEQ ID No:88) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STX1A" encoded by a nucleic acid that hybridizes to the "STX1A" nucleic acid or its complement under low stringency conditions, and/or

(Ixvii) "SUCLA2" (SEQ ID No:89) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SUCLA2" encoded by a nucleic acid that hybridizes to the "SUCLA2" nucleic acid or its complement under low stringency conditions, and/or

(Ixviii) "Serine/threonine protein phosphatase 6" (SEQ ID No:90) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Serine/threonine protein phosphatase 6" encoded by a nucleic acid that hybridizes to the "Serine/threonine protein phosphatase 6" nucleic acid or its complement under low stringency conditions, and/or

(Ixi) "Sortilin-related receptor " (SEQ ID No:91) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sortilin-related receptor " encoded by a nucleic acid that hybridizes to the "Sortilin-related receptor " nucleic acid or its complement under low stringency conditions, and/or

(Ixx) "Synaptogyrin 3" (SEQ ID No:92) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Synaptogyrin 3" encoded by a nucleic acid that hybridizes to the "Synaptogyrin 3" nucleic acid or its complement under low stringency conditions, and/or

(Ixxi) "TYK2" (SEQ ID No:93) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TYK2" encoded by a nucleic acid that hybridizes to the "TYK2" nucleic acid or its complement under low stringency conditions, and/or

(Ixxii) "Ubiquitin-protein ligase E3-alpha" (SEQ ID No:94) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Ubiquitin-protein ligase E3-alpha" encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase E3-alpha" nucleic acid or its complement under low stringency conditions, and/or

(Ixxiii) "VGF nerve growth factor inducible protein" (SEQ ID No:95) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "VGF nerve growth factor inducible protein" encoded by a nucleic acid that hybridizes to the "VGF nerve growth factor inducible protein" nucleic acid or its complement under low stringency conditions, and/or

(Ixxiv) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions, and/or

(Ixxv) "Zinc finger protein 198" (SEQ ID No:97) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Zinc finger protein 198" encoded by a nucleic acid that hybridizes to the "Zinc finger protein 198" nucleic acid or its complement under low stringency conditions, and/or

(Ixxvi) "hypothetical protein MGC13186" (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC13186" encoded by a nucleic acid that hybridizes to

the "hypothetical protein MGC13186" nucleic acid or its complement under low stringency conditions, and/or

(lxxvii) "similar to SD27354p [*Drosophila melanogaster*] " (SEQ ID No:99) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "similar to SD27354p [*Drosophila melanogaster*] " encoded by a nucleic acid that hybridizes to the "similar to SD27354p [*Drosophila melanogaster*] " nucleic acid or its complement under low stringency conditions, is present in the complex.

32. The method of any of No. 26 - 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease; inflammatory conditions such as ulcerative colitis, Crohn's disease and arteriosclerosis.

33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 - 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease; inflammatory conditions such as ulcerative colitis, Crohn's disease and arteriosclerosis.

34. A method for the production of a pharmaceutical composition comprising carrying out the method of any of No. 1 - 8 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.

35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, activity of, or component composition of, or intracellular localization of the complex of any one of the No. 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity,

or protein components of, said complex in an analogous sample from a subject not having the disease or disorder or predisposition indicates the presence in the subject of the disease or disorder or predisposition in the subject.

36. The method of No. 35, wherein the amount of said complex is determined.

37. The method of No. 35, wherein the activity of said complex is determined.

38. The method of No. 37, wherein said determining step comprises isolating from the subject said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.

39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.

40. The method of No. 39, wherein said determining step comprises determining whether  
(i) "ADAMTS-19" (SEQ ID No:25) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ADAMTS-19" encoded by a nucleic acid that hybridizes to the "ADAMTS-19" nucleic acid or its complement under low stringency conditions, and/or

(ii) "APLP1" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions, and/or

(iii) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions, and/or

(iv) "Axonemal dynein heavy chain 8" (SEQ ID No:26) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Axonemal dynein heavy chain 8" encoded by a nucleic acid that hybridizes to the



"Axonemal dynein heavy chain 8" nucleic acid or its complement under low stringency conditions, and/or

(v) "BAT1" (SEQ ID No:27) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BAT1" encoded by a nucleic acid that hybridizes to the "BAT1" nucleic acid or its complement under low stringency conditions, and/or

(vi) "C20orf11 (sim to a region of RANBPM)" (SEQ ID No:28) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "C20orf11 (sim to a region of RANBPM)" encoded by a nucleic acid that hybridizes to the "C20orf11 (sim to a region of RANBPM)" nucleic acid or its complement under low stringency conditions, and/or

(vii) "CGB0\_HUMAN" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGB0\_HUMAN" encoded by a nucleic acid that hybridizes to the "CGB0\_HUMAN" nucleic acid or its complement under low stringency conditions, and/or

(viii) "Cadherin EGF LAG seven-pass G-type receptor 2" (SEQ ID No:30) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2" encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2" nucleic acid or its complement under low stringency conditions, and/or

(ix) "Calsyntenin-1" (SEQ ID No:31) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-1" encoded by a nucleic acid that hybridizes to the "Calsyntenin-1" nucleic acid or its complement under low stringency conditions, and/or

(x) "Calsyntenin-2" (SEQ ID No:32) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-2" encoded by a nucleic acid that hybridizes to the "Calsyntenin-2" nucleic acid or its complement under low stringency conditions, and/or

(xi) "Calsyntenin-3" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-3" encoded by a nucleic acid that hybridizes to the "Calsyntenin-3" nucleic acid or its complement under low stringency conditions, and/or

(xii) "Chondroitin sulfate proteoglycan 6" (SEQ ID No:34) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a

variant of "Chondroitin sulfate proteoglycan 6" encoded by a nucleic acid that hybridizes to the "Chondroitin sulfate proteoglycan 6" nucleic acid or its complement under low stringency conditions, and/or

(xiii) "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" (SEQ ID No:35) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" encoded by a nucleic acid that hybridizes to the "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" nucleic acid or its complement under low stringency conditions, and/or

(xiv) "DC6 protein" (SEQ ID No:36) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DC6 protein" encoded by a nucleic acid that hybridizes to the "DC6 protein" nucleic acid or its complement under low stringency conditions, and/or.

(xv) "Dkfzp586c1924" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dkfzp586c1924" encoded by a nucleic acid that hybridizes to the "Dkfzp586c1924" nucleic acid or its complement under low stringency conditions, and/or

(xvi) "Dynein light chain 2A " (SEQ ID No:38) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynein light chain 2A " encoded by a nucleic acid that hybridizes to the "Dynein light chain 2A " nucleic acid or its complement under low stringency conditions, and/or

(xvii) "Dynein light chain-A" (SEQ ID No:39) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynein light chain-A" encoded by a nucleic acid that hybridizes to the "Dynein light chain-A" nucleic acid or its complement under low stringency conditions, and/or

(xviii) "ELAVL3" (SEQ ID No:40) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ELAVL3" encoded by a nucleic acid that hybridizes to the "ELAVL3" nucleic acid or its complement under low stringency conditions, and/or

(xix) "ENG00000168820 (hypothetical protein with p-loop)" (SEQ ID No:41) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENG00000168820 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ENG00000168820 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions, and/or

- (xx) "Eukaryotic translation initiation factor 4A, isoform" (SEQ ID No:42) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Eukaryotic translation initiation factor 4A, isoform" encoded by a nucleic acid that hybridizes to the "Eukaryotic translation initiation factor 4A, isoform" nucleic acid or its complement under low stringency conditions, and/or
- (xxi) "FLJ13910" (SEQ ID No:43) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13910" encoded by a nucleic acid that hybridizes to the "FLJ13910" nucleic acid or its complement under low stringency conditions, and/or
- (xxii) "FRAP1" (SEQ ID No:44) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FRAP1" encoded by a nucleic acid that hybridizes to the "FRAP1" nucleic acid or its complement under low stringency conditions, and/or
- (xxiii) "Filamin, gamma" (SEQ ID No:45) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Filamin, gamma" encoded by a nucleic acid that hybridizes to the "Filamin, gamma" nucleic acid or its complement under low stringency conditions, and/or
- (xxiv) "GTP-binding protein ERA" (SEQ ID No:46) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GTP-binding protein ERA" encoded by a nucleic acid that hybridizes to the "GTP-binding protein ERA" nucleic acid or its complement under low stringency conditions, and/or
- (xxv) "HADH2/ERAB (mitochondrial enzyme)" (SEQ ID No:47) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HADH2/ERAB (mitochondrial enzyme)" encoded by a nucleic acid that hybridizes to the "HADH2/ERAB (mitochondrial enzyme)" nucleic acid or its complement under low stringency conditions, and/or
- (xxvi) "HDAC2" (SEQ ID No:48) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HDAC2" encoded by a nucleic acid that hybridizes to the "HDAC2" nucleic acid or its complement under low stringency conditions, and/or
- (xxvii) "HERC2 protein" (SEQ ID No:49) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HERC2

protein" encoded by a nucleic acid that hybridizes to the "HERC2 protein" nucleic acid or its complement under low stringency conditions, and/or

(xxviii) "HSPC154" (SEQ ID No:50) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC154" encoded by a nucleic acid that hybridizes to the "HSPC154" nucleic acid or its complement under low stringency conditions, and/or

(xxix) "HSPC245" (SEQ ID No:51) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC245" encoded by a nucleic acid that hybridizes to the "HSPC245" nucleic acid or its complement under low stringency conditions, and/or

(xxx) "HYPOTHETICAL PROTEIN FLJ10618" (SEQ ID No:52) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ10618" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ10618" nucleic acid or its complement under low stringency conditions, and/or

(xxxi) "HYPOTHETICAL PROTEIN FLJ12599" (SEQ ID No:53) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ12599" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ12599" nucleic acid or its complement under low stringency conditions, and/or

(xxxii) "Hunc18a" (SEQ ID No:54) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hunc18a" encoded by a nucleic acid that hybridizes to the "Hunc18a" nucleic acid or its complement under low stringency conditions, and/or

(xxxiii) "Hypothetical protein FLJ10795" (SEQ ID No:55) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ10795" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ10795" nucleic acid or its complement under low stringency conditions, and/or

(xxxiv) "Hypothetical protein FLJ20397" (SEQ ID No:56) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ20397" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ20397" nucleic acid or its complement under low stringency conditions, and/or

(xxxv) "IKAP" (SEQ ID No:57) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IKAP" encoded by a nucleic acid that hybridizes to the "IKAP" nucleic acid or its complement under low stringency conditions, and/or

(xxxvi) "Insulinoma-glucagonoma protein 20" (SEQ ID No:58) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Insulinoma-glucagonoma protein 20" encoded by a nucleic acid that hybridizes to the "Insulinoma-glucagonoma protein 20" nucleic acid or its complement under low stringency conditions, and/or

(xxxvii) "KIAA0056" (SEQ ID No:59) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0056" encoded by a nucleic acid that hybridizes to the "KIAA0056" nucleic acid or its complement under low stringency conditions, and/or

(xxxviii) "KIAA0166" (SEQ ID No:60) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0166" encoded by a nucleic acid that hybridizes to the "KIAA0166" nucleic acid or its complement under low stringency conditions, and/or

(xxxix) "KIAA0325 (FRAGMENT)" (SEQ ID No:61) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0325 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0325 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or

(xl) "KIAA0564" (SEQ ID No:62) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0564" encoded by a nucleic acid that hybridizes to the "KIAA0564" nucleic acid or its complement under low stringency conditions, and/or

(xli) "KIAA0763" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions, and/or

(xlii) "LIB ( leucine-rich repeat protein)" (SEQ ID No:64) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LIB ( leucine-rich repeat protein)" encoded by a nucleic acid that hybridizes to the "LIB ( leucine-rich repeat protein)" nucleic acid or its complement under low stringency conditions, and/or

(xlili) "Laminin, gamma 1 " (SEQ ID No:65) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Laminin, gamma 1 " encoded by a nucleic acid that hybridizes to the "Laminin, gamma 1 " nucleic acid or its complement under low stringency conditions, and/or

(xliv) "MBIP" (SEQ ID No:66) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MBIP" encoded by a nucleic acid that hybridizes to the "MBIP" nucleic acid or its complement under low stringency conditions, and/or

(xlv) "MEGF7 (FRAGMENT)" (SEQ ID No:67) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MEGF7 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "MEGF7 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or

(xlvi) "MT-ACT48" (SEQ ID No:68) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MT-ACT48" encoded by a nucleic acid that hybridizes to the "MT-ACT48" nucleic acid or its complement under low stringency conditions, and/or

(xlvii) "Myosin IXB" (SEQ ID No:69) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Myosin IXB" encoded by a nucleic acid that hybridizes to the "Myosin IXB" nucleic acid or its complement under low stringency conditions, and/or

(xlviii) "NEU1" (SEQ ID No:70) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NEU1" encoded by a nucleic acid that hybridizes to the "NEU1" nucleic acid or its complement under low stringency conditions, and/or

(xlix) "NIPSNAP1" (SEQ ID No:71) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NIPSNAP1" encoded by a nucleic acid that hybridizes to the "NIPSNAP1" nucleic acid or its complement under low stringency conditions, and/or

(l) "NIPSNAP2" (SEQ ID No:72) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NIPSNAP2" encoded by a nucleic acid that hybridizes to the "NIPSNAP2" nucleic acid or its complement under low stringency conditions, and/or

(li) "Neurexin-1" (SEQ ID No:73) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurexin-1"

encoded by a nucleic acid that hybridizes to the "Neurexin-1" nucleic acid or its complement under low stringency conditions, and/or

(lii) "PDZ and LIM domain protein 1" (SEQ ID No:74) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PDZ and LIM domain protein 1" encoded by a nucleic acid that hybridizes to the "PDZ and LIM domain protein 1" nucleic acid or its complement under low stringency conditions, and/or

(liii) "PILB" (SEQ ID No:75) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PILB" encoded by a nucleic acid that hybridizes to the "PILB" nucleic acid or its complement under low stringency conditions, and/or

(liv) "PILT" (SEQ ID No:76) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PILT" encoded by a nucleic acid that hybridizes to the "PILT" nucleic acid or its complement under low stringency conditions, and/or

(lv) "Paladin" (SEQ ID No:77) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Paladin" encoded by a nucleic acid that hybridizes to the "Paladin" nucleic acid or its complement under low stringency conditions, and/or

(lvi) "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" (SEQ ID No:78) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" encoded by a nucleic acid that hybridizes to the "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" nucleic acid or its complement under low stringency conditions, and/or

(lvii) "Procollagen C-endopeptidase enhancer" (SEQ ID No:79) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Procollagen C-endopeptidase enhancer" encoded by a nucleic acid that hybridizes to the "Procollagen C-endopeptidase enhancer" nucleic acid or its complement under low stringency conditions, and/or

(lviii) "Programmed cell death 10" (SEQ ID No:80) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Programmed cell death 10" encoded by a nucleic acid that hybridizes to the "Programmed cell death 10" nucleic acid or its complement under low stringency conditions, and/or

(lix) "Protein similar to AGCP6688" (SEQ ID No:81) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to AGCP6688" encoded by a nucleic acid that hybridizes to the "Protein similar to AGCP6688" nucleic acid or its complement under low stringency conditions, and/or

(lx) "RAB7L1" (SEQ ID No:82) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB7L1" encoded by a nucleic acid that hybridizes to the "RAB7L1" nucleic acid or its complement under low stringency conditions, and/or

(lxi) "RANBP1" (SEQ ID No:83) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RANBP1" encoded by a nucleic acid that hybridizes to the "RANBP1" nucleic acid or its complement under low stringency conditions, and/or

(lxii) "RPGR-interacting protein 1" (SEQ ID No:84) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RPGR-interacting protein 1" encoded by a nucleic acid that hybridizes to the "RPGR-interacting protein 1" nucleic acid or its complement under low stringency conditions, and/or

(lxiii) "Reelin" (SEQ ID No:85) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Reelin" encoded by a nucleic acid that hybridizes to the "Reelin" nucleic acid or its complement under low stringency conditions, and/or

(lxiv) "SNAP-25" (SEQ ID No:86) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SNAP-25" encoded by a nucleic acid that hybridizes to the "SNAP-25" nucleic acid or its complement under low stringency conditions, and/or

(lxv) "STMN3" (SEQ ID No:87) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STMN3" encoded by a nucleic acid that hybridizes to the "STMN3" nucleic acid or its complement under low stringency conditions, and/or

(lxvi) "STX1A" (SEQ ID No:88) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STX1A" encoded by a nucleic acid that hybridizes to the "STX1A" nucleic acid or its complement under low stringency conditions, and/or



(Ixxvii) "SUCLA2" (SEQ ID No:89) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SUCLA2" encoded by a nucleic acid that hybridizes to the "SUCLA2" nucleic acid or its complement under low stringency conditions, and/or

(Ixxviii) "Serine/threonine protein phosphatase 6" (SEQ ID No:90) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Serine/threonine protein phosphatase 6" encoded by a nucleic acid that hybridizes to the "Serine/threonine protein phosphatase 6" nucleic acid or its complement under low stringency conditions, and/or

(Ixxix) "Sortilin-related receptor " (SEQ ID No:91) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sortilin-related receptor " encoded by a nucleic acid that hybridizes to the "Sortilin-related receptor " nucleic acid or its complement under low stringency conditions, and/or

(Ixxx) "Synaptogyrin 3" (SEQ ID No:92) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Synaptogyrin 3" encoded by a nucleic acid that hybridizes to the "Synaptogyrin 3" nucleic acid or its complement under low stringency conditions, and/or

(Ixxxi) "TYK2" (SEQ ID No:93) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TYK2" encoded by a nucleic acid that hybridizes to the "TYK2" nucleic acid or its complement under low stringency conditions, and/or

(Ixxxii) "Ubiquitin-protein ligase E3-alpha" (SEQ ID No:94) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Ubiquitin-protein ligase E3-alpha" encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase E3-alpha" nucleic acid or its complement under low stringency conditions, and/or

(Ixxxiii) "VGF nerve growth factor inducible protein" (SEQ ID No:95) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "VGF nerve growth factor inducible protein" encoded by a nucleic acid that hybridizes to the "VGF nerve growth factor inducible protein" nucleic acid or its complement under low stringency conditions, and/or

(Ixxxiv) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta"

encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions, and/or

(lxxv) "Zinc finger protein 198" (SEQ ID No:97) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Zinc finger protein 198" encoded by a nucleic acid that hybridizes to the "Zinc finger protein 198" nucleic acid or its complement under low stringency conditions, and/or

(lxxvi) "hypothetical protein MGC13186" (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC13186" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC13186" nucleic acid or its complement under low stringency conditions, and/or

(lxxvii) "similar to SD27354p [Drosophila melanogaster] " (SEQ ID No:99) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "similar to SD27354p [Drosophila melanogaster] " encoded by a nucleic acid that hybridizes to the "similar to SD27354p [Drosophila melanogaster] " nucleic acid or its complement under low stringency conditions, is present in the complex.

41. The complex of any one of No. 1 - 8, or proteins of No. 13 or the antibody or fragment of No. 17, for use in a method of diagnosing a disease or disorder such as neurodegenerative disease such as Alzheimer's disease; inflammatory conditions such as ulcerative colitis, Crohn's disease and atherosclerosis.

42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity or component composition of or intracellular localization of, the complex of anyone of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, the transactivation of reporter genes by APP-Gal4/VP16 (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or

transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), or protein components of, said complex.

43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.

44. The method according to No. 42, wherein said disease or disorder involves increased levels of the amount or activity of said complex.

45. Complex of any of No. 1 - 8 and/or protein selected from the following proteins  
(i) "ADAMTS-19" (SEQ ID No:25) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ADAMTS-19" encoded by a nucleic acid that hybridizes to the "ADAMTS-19" nucleic acid or its complement under low stringency conditions,

(ii) "APLP1" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions,

(iii) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,

(iv) "Axonemal dynein heavy chain 8" (SEQ ID No:26) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Axonemal dynein heavy chain 8" encoded by a nucleic acid that hybridizes to the "Axonemal dynein heavy chain 8" nucleic acid or its complement under low stringency conditions,

(v) "BAT1" (SEQ ID No:27) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BAT1" encoded by a

nucleic acid that hybridizes to the "BAT1" nucleic acid or its complement under low stringency conditions,

- (vi) "C20orf11 (sim to a region of RANBPM)" (SEQ ID No:28) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "C20orf11 (sim to a region of RANBPM)" encoded by a nucleic acid that hybridizes to the "C20orf11 (sim to a region of RANBPM)" nucleic acid or its complement under low stringency conditions,
- (vii) "CGB0\_HUMAN" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGB0\_HUMAN" encoded by a nucleic acid that hybridizes to the "CGB0\_HUMAN" nucleic acid or its complement under low stringency conditions,
- (viii) "Cadherin EGF LAG seven-pass G-type receptor 2" (SEQ ID No:30) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2" encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2" nucleic acid or its complement under low stringency conditions,
- (ix) "Calsyntenin-1" (SEQ ID No:31) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-1" encoded by a nucleic acid that hybridizes to the "Calsyntenin-1" nucleic acid or its complement under low stringency conditions,
- (x) "Calsyntenin-2" (SEQ ID No:32) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-2" encoded by a nucleic acid that hybridizes to the "Calsyntenin-2" nucleic acid or its complement under low stringency conditions,
- (xi) "Calsyntenin-3" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-3" encoded by a nucleic acid that hybridizes to the "Calsyntenin-3" nucleic acid or its complement under low stringency conditions,
- (xii) "Chondroitin sulfate proteoglycan 6" (SEQ ID No:34) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Chondroitin sulfate proteoglycan 6" encoded by a nucleic acid that hybridizes to the "Chondroitin sulfate proteoglycan 6" nucleic acid or its complement under low stringency conditions,

- (xiii) "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" (SEQ ID No:35) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" encoded by a nucleic acid that hybridizes to the "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" nucleic acid or its complement under low stringency conditions,
- (xiv) "DC6 protein" (SEQ ID No:36) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DC6 protein" encoded by a nucleic acid that hybridizes to the "DC6 protein" nucleic acid or its complement under low stringency conditions,
- (xv) "Dkfzp586c1924" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dkfzp586c1924" encoded by a nucleic acid that hybridizes to the "Dkfzp586c1924" nucleic acid or its complement under low stringency conditions,
- (xvi) "Dynein light chain 2A " (SEQ ID No:38) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynein light chain 2A " encoded by a nucleic acid that hybridizes to the "Dynein light chain 2A " nucleic acid or its complement under low stringency conditions,
- (xvii) "Dynein light chain-A" (SEQ ID No:39) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynein light chain-A" encoded by a nucleic acid that hybridizes to the "Dynein light chain-A" nucleic acid or its complement under low stringency conditions,
- (xviii) "ELAVL3" (SEQ ID No:40) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ELAVL3" encoded by a nucleic acid that hybridizes to the "ELAVL3" nucleic acid or its complement under low stringency conditions,
- (xix) "ENG00000168820 (hypothetical protein with p-loop)" (SEQ ID No:41) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENG00000168820 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ENG00000168820 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions,
- (xx) "Eukaryotic translation initiation factor 4A, isoform" (SEQ ID No:42) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Eukaryotic translation initiation factor 4A, isoform" encoded by a nucleic

acid that hybridizes to the "Eukaryotic translation initiation factor 4A, isoform" nucleic acid or its complement under low stringency conditions,

(xxi) "FLJ13910" (SEQ ID No:43) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13910" encoded by a nucleic acid that hybridizes to the "FLJ13910" nucleic acid or its complement under low stringency conditions,

(xxii) "FRAP1" (SEQ ID No:44) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FRAP1" encoded by a nucleic acid that hybridizes to the "FRAP1" nucleic acid or its complement under low stringency conditions,

(xxiii) "Filamin, gamma" (SEQ ID No:45) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Filamin, gamma" encoded by a nucleic acid that hybridizes to the "Filamin, gamma" nucleic acid or its complement under low stringency conditions,

(xxiv) "GTP-binding protein ERA" (SEQ ID No:46) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GTP-binding protein ERA" encoded by a nucleic acid that hybridizes to the "GTP-binding protein ERA" nucleic acid or its complement under low stringency conditions,

(xxv) "HADH2/ERAB (mitochondrial enzyme)" (SEQ ID No:47) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HADH2/ERAB (mitochondrial enzyme)" encoded by a nucleic acid that hybridizes to the "HADH2/ERAB (mitochondrial enzyme)" nucleic acid or its complement under low stringency conditions,

(xxvi) "HDAC2" (SEQ ID No:48) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HDAC2" encoded by a nucleic acid that hybridizes to the "HDAC2" nucleic acid or its complement under low stringency conditions,

(xxvii) "HERC2 protein" (SEQ ID No:49) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HERC2 protein" encoded by a nucleic acid that hybridizes to the "HERC2 protein" nucleic acid or its complement under low stringency conditions,

(xxviii) "HSPC154" (SEQ ID No:50) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC154"

encoded by a nucleic acid that hybridizes to the "HSPC154" nucleic acid or its complement under low stringency conditions,

(xxix) "HSPC245" (SEQ ID No:51) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC245" encoded by a nucleic acid that hybridizes to the "HSPC245" nucleic acid or its complement under low stringency conditions,

(xxx) "HYPOTHETICAL PROTEIN FLJ10618" (SEQ ID No:52) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ10618" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ10618" nucleic acid or its complement under low stringency conditions,

(xxxi) "HYPOTHETICAL PROTEIN FLJ12599" (SEQ ID No:53) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ12599" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ12599" nucleic acid or its complement under low stringency conditions,

(xxxii) "Hunc18a" (SEQ ID No:54) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hunc18a" encoded by a nucleic acid that hybridizes to the "Hunc18a" nucleic acid or its complement under low stringency conditions,

(xxxiii) "Hypothetical protein FLJ10795" (SEQ ID No:55) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ10795" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ10795" nucleic acid or its complement under low stringency conditions,

(xxxiv) "Hypothetical protein FLJ20397" (SEQ ID No:56) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ20397" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ20397" nucleic acid or its complement under low stringency conditions,

(xxxv) "IKAP" (SEQ ID No:57) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IKAP" encoded by a nucleic acid that hybridizes to the "IKAP" nucleic acid or its complement under low stringency conditions,

(xxxvi) "Insulinoma-glucagonoma protein 20" (SEQ ID No:58) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Insulinoma-glucagonoma protein 20" encoded by a nucleic acid that hybridizes to the "Insulinoma-glucagonoma protein 20" nucleic acid or its complement under low stringency conditions,

(xxxvii) "KIAA0056" (SEQ ID No:59) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0056" encoded by a nucleic acid that hybridizes to the "KIAA0056" nucleic acid or its complement under low stringency conditions,

(xxxviii) "KIAA0166" (SEQ ID No:60) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0166" encoded by a nucleic acid that hybridizes to the "KIAA0166" nucleic acid or its complement under low stringency conditions,

(xxxix) "KIAA0325 (FRAGMENT)" (SEQ ID No:61) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0325 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0325 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xl) "KIAA0564" (SEQ ID No:62) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0564" encoded by a nucleic acid that hybridizes to the "KIAA0564" nucleic acid or its complement under low stringency conditions,

(xli) "KIAA0763" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions,

(xlii) "LIB ( leucine-rich repeat protein)" (SEQ ID No:64) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LIB ( leucine-rich repeat protein)" encoded by a nucleic acid that hybridizes to the "LIB ( leucine-rich repeat protein)" nucleic acid or its complement under low stringency conditions,

(xlili) "Laminin, gamma 1 " (SEQ ID No:65) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Laminin, gamma 1 " encoded by a nucleic acid that hybridizes to the "Laminin, gamma 1 " nucleic acid or its complement under low stringency conditions,



- (xlv) "MBIP" (SEQ ID No:66) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MBIP" encoded by a nucleic acid that hybridizes to the "MBIP" nucleic acid or its complement under low stringency conditions,
- (xlv) "MEGF7 (FRAGMENT)" (SEQ ID No:67) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MEGF7 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "MEGF7 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (xlvi) "MT-ACT48" (SEQ ID No:68) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MT-ACT48" encoded by a nucleic acid that hybridizes to the "MT-ACT48" nucleic acid or its complement under low stringency conditions,
- (xlvii) "Myosin IXB" (SEQ ID No:69) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Myosin IXB" encoded by a nucleic acid that hybridizes to the "Myosin IXB" nucleic acid or its complement under low stringency conditions,
- (xlviii) "NEU1" (SEQ ID No:70) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NEU1" encoded by a nucleic acid that hybridizes to the "NEU1" nucleic acid or its complement under low stringency conditions,
- (xlix) "NIPSNAP1" (SEQ ID No:71) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NIPSNAP1" encoded by a nucleic acid that hybridizes to the "NIPSNAP1" nucleic acid or its complement under low stringency conditions,
- (l) "NIPSNAP2" (SEQ ID No:72) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NIPSNAP2" encoded by a nucleic acid that hybridizes to the "NIPSNAP2" nucleic acid or its complement under low stringency conditions,
- (li) "Neurexin-1" (SEQ ID No:73) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurexin-1" encoded by a nucleic acid that hybridizes to the "Neurexin-1" nucleic acid or its complement under low stringency conditions,
- (lii) "PDZ and LIM domain protein 1" (SEQ ID No:74) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"PDZ and LIM domain protein 1" encoded by a nucleic acid that hybridizes to the "PDZ and LIM domain protein 1" nucleic acid or its complement under low stringency conditions,

(liii) "PILB" (SEQ ID No:75) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PILB" encoded by a nucleic acid that hybridizes to the "PILB" nucleic acid or its complement under low stringency conditions,

(liv) "PILT" (SEQ ID No:76) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PILT" encoded by a nucleic acid that hybridizes to the "PILT" nucleic acid or its complement under low stringency conditions,

(lv) "Paladin" (SEQ ID No:77) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Paladin" encoded by a nucleic acid that hybridizes to the "Paladin" nucleic acid or its complement under low stringency conditions,

(lvi) "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" (SEQ ID No:78) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" encoded by a nucleic acid that hybridizes to the "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" nucleic acid or its complement under low stringency conditions,

(lvii) "Procollagen C-endopeptidase enhancer" (SEQ ID No:79) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Procollagen C-endopeptidase enhancer" encoded by a nucleic acid that hybridizes to the "Procollagen C-endopeptidase enhancer" nucleic acid or its complement under low stringency conditions,

(lviii) "Programmed cell death 10" (SEQ ID No:80) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Programmed cell death 10" encoded by a nucleic acid that hybridizes to the "Programmed cell death 10" nucleic acid or its complement under low stringency conditions,

(lix) "Protein similar to AGCP6688" (SEQ ID No:81) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to AGCP6688" encoded by a nucleic acid that hybridizes to the "Protein similar to AGCP6688" nucleic acid or its complement under low stringency conditions,

- (ix) "RAB7L1" (SEQ ID No:82) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB7L1" encoded by a nucleic acid that hybridizes to the "RAB7L1" nucleic acid or its complement under low stringency conditions,
- (lxi) "RANBP1" (SEQ ID No:83) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RANBP1" encoded by a nucleic acid that hybridizes to the "RANBP1" nucleic acid or its complement under low stringency conditions,
- (lxii) "RPGR-interacting protein 1" (SEQ ID No:84) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RPGR-interacting protein 1" encoded by a nucleic acid that hybridizes to the "RPGR-interacting protein 1" nucleic acid or its complement under low stringency conditions,
- (lxiii) "Reelin" (SEQ ID No:85) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Reelin" encoded by a nucleic acid that hybridizes to the "Reelin" nucleic acid or its complement under low stringency conditions,
- (lxiv) "SNAP-25" (SEQ ID No:86) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SNAP-25" encoded by a nucleic acid that hybridizes to the "SNAP-25" nucleic acid or its complement under low stringency conditions,
- (lxv) "STMN3" (SEQ ID No:87) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STMN3" encoded by a nucleic acid that hybridizes to the "STMN3" nucleic acid or its complement under low stringency conditions,
- (lxvi) "STX1A" (SEQ ID No:88) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STX1A" encoded by a nucleic acid that hybridizes to the "STX1A" nucleic acid or its complement under low stringency conditions,
- (lxvii) "SUCLA2" (SEQ ID No:89) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SUCLA2" encoded by a nucleic acid that hybridizes to the "SUCLA2" nucleic acid or its complement under low stringency conditions,
- (lxviii) "Serine/threonine protein phosphatase 6" (SEQ ID No:90) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a

variant of "Serine/threonine protein phosphatase 6" encoded by a nucleic acid that hybridizes to the "Serine/threonine protein phosphatase 6" nucleic acid or its complement under low stringency conditions,

(lxxix) "Sortilin-related receptor " (SEQ ID No:91) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sortilin-related receptor " encoded by a nucleic acid that hybridizes to the "Sortilin-related receptor " nucleic acid or its complement under low stringency conditions,

(lxxx) "Synaptogyrin 3" (SEQ ID No:92) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Synaptogyrin 3" encoded by a nucleic acid that hybridizes to the "Synaptogyrin 3" nucleic acid or its complement under low stringency conditions,

(lxxxi) "TYK2" (SEQ ID No:93) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TYK2" encoded by a nucleic acid that hybridizes to the "TYK2" nucleic acid or its complement under low stringency conditions,

(lxxxii) "Ubiquitin-protein ligase E3-alpha" (SEQ ID No:94) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Ubiquitin-protein ligase E3-alpha" encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase E3-alpha" nucleic acid or its complement under low stringency conditions,

(lxxxiii) "VGF nerve growth factor inducible protein" (SEQ ID No:95) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "VGF nerve growth factor inducible protein" encoded by a nucleic acid that hybridizes to the "VGF nerve growth factor inducible protein" nucleic acid or its complement under low stringency conditions,

(lxxxiv) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions,

(lxxxv) "Zinc finger protein 198" (SEQ ID No:97) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Zinc finger protein 198" encoded by a nucleic acid that hybridizes to the "Zinc finger protein 198" nucleic acid or its complement under low stringency conditions,

(lxxvi) "hypothetical protein MGC13186" (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC13186" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC13186" nucleic acid or its complement under low stringency conditions, and/or(lxxvii) "similar to SD27354p [*Drosophila melanogaster*] " (SEQ ID No:99) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "similar to SD27354p [*Drosophila melanogaster*] " encoded by a nucleic acid that hybridizes to the "similar to SD27354p [*Drosophila melanogaster*] " nucleic acid or its complement under low stringency conditions, as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease; inflammatory conditions such as ulcerative colitis, Crohn's disease and atherosclerosis.

The present invention further relates to the following embodiments of the Presenilin-2 complex

1. A protein complex selected from complex (I) and comprising
  - (a) at least one first protein selected from the group consisting of:
    - (i) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,
    - (ii) "DOCK3" (SEQ ID No:123) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DOCK3" encoded by a nucleic acid that hybridizes to the "DOCK3" nucleic acid or its complement under low stringency conditions,
    - (iii) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions, and
    - (iv) "Presenilin 2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 2"

encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions, and

(b) at least one second protein, which second protein is selected from the group consisting of:

- (i) "18 kDa microsomal signal peptidase subunit" (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "18 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,
- (ii) "200 kDa proteasome activator" (SEQ ID No:101) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "200 kDa proteasome activator" encoded by a nucleic acid that hybridizes to the "200 kDa proteasome activator" nucleic acid or its complement under low stringency conditions,
- (iii) "ABCB11" (SEQ ID No:102) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ABCB11" encoded by a nucleic acid that hybridizes to the "ABCB11" nucleic acid or its complement under low stringency conditions,
- (iv) "ATM" (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATM" encoded by a nucleic acid that hybridizes to the "ATM" nucleic acid or its complement under low stringency conditions,
- (v) "ATP-binding cassette protein, sub-family B, member 1" (SEQ ID No:104) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette protein, sub-family B, member 1" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette protein, sub-family B, member 1" nucleic acid or its complement under low stringency conditions,
- (vi) "ATP-dependent metalloprotease FtsH1 homolog" (SEQ ID No:105) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-dependent metalloprotease FtsH1 homolog" encoded by a nucleic acid that hybridizes to the "ATP-dependent metalloprotease FtsH1 homolog" nucleic acid or its complement under low stringency conditions,
- (vii) "ATP7A" (SEQ ID No:106) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP7A" encoded by a

nucleic acid that hybridizes to the "ATP7A" nucleic acid or its complement under low stringency conditions,

(viii) "Acetolactate synthase homolog" (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Acetolactate synthase homolog" encoded by a nucleic acid that hybridizes to the "Acetolactate synthase homolog" nucleic acid or its complement under low stringency conditions,

(ix) "Adrenoleukodystrophy protein" (SEQ ID No:108) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Adrenoleukodystrophy protein" encoded by a nucleic acid that hybridizes to the "Adrenoleukodystrophy protein" nucleic acid or its complement under low stringency conditions,

(x) "BIG1" (SEQ ID No:110) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BIG1" encoded by a nucleic acid that hybridizes to the "BIG1" nucleic acid or its complement under low stringency conditions,

(xi) "BTAF1" (SEQ ID No:111) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BTAF1" encoded by a nucleic acid that hybridizes to the "BTAF1" nucleic acid or its complement under low stringency conditions,

(xii) "CD97" (SEQ ID No:112) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CD97" encoded by a nucleic acid that hybridizes to the "CD97" nucleic acid or its complement under low stringency conditions,

(xiii) "CDM\_HUMAN" (SEQ ID No:113) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDM\_HUMAN" encoded by a nucleic acid that hybridizes to the "CDM\_HUMAN" nucleic acid or its complement under low stringency conditions,

(xiv) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,

(xv) "CGI-51" (SEQ ID No:115) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-51" encoded by a

nucleic acid that hybridizes to the "CGI-51" nucleic acid or its complement under low stringency conditions,

(xvi) "CHRNA3" (SEQ ID No:116) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CHRNA3" encoded by a nucleic acid that hybridizes to the "CHRNA3" nucleic acid or its complement under low stringency conditions,

(xvii) "Calcium-binding protein P22" (SEQ ID No:117) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calcium-binding protein P22" encoded by a nucleic acid that hybridizes to the "Calcium-binding protein P22" nucleic acid or its complement under low stringency conditions,

(xviii) "Cation-chloride cotransporter-interacting protein" (SEQ ID No:118) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cation-chloride cotransporter-interacting protein" encoded by a nucleic acid that hybridizes to the "Cation-chloride cotransporter-interacting protein" nucleic acid or its complement under low stringency conditions,

(xix) "Centromere/kinetochore protein ZW10 homolog" (SEQ ID No:119) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Centromere/kinetochore protein ZW10 homolog" encoded by a nucleic acid that hybridizes to the "Centromere/kinetochore protein ZW10 homolog" nucleic acid or its complement under low stringency conditions,

(xx) "Cerebral protein 10" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cerebral protein 10" encoded by a nucleic acid that hybridizes to the "Cerebral protein 10" nucleic acid or its complement under low stringency conditions,

(xxi) "DAAM1" (SEQ ID No:121) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DAAM1" encoded by a nucleic acid that hybridizes to the "DAAM1" nucleic acid or its complement under low stringency conditions,

(xxii) "DAPK1" (SEQ ID No:122) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DAPK1" encoded by a nucleic acid that hybridizes to the "DAPK1" nucleic acid or its complement under low stringency conditions,

(xxiii) "DKFZp586c1924" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of



- "DKFZp586c1924" encoded by a nucleic acid that hybridizes to the "DKFZp586c1924" nucleic acid or its complement under low stringency conditions,
- (xxiv) "Down syndrome critical region protein 2" (SEQ ID No:124) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Down syndrome critical region protein 2" encoded by a nucleic acid that hybridizes to the "Down syndrome critical region protein 2" nucleic acid or its complement under low stringency conditions,
- (xxv) "ECSIT" (SEQ ID No:125) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ECSIT" encoded by a nucleic acid that hybridizes to the "ECSIT" nucleic acid or its complement under low stringency conditions,
- (xxvi) "FACL1" (SEQ ID No:126) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FACL1" encoded by a nucleic acid that hybridizes to the "FACL1" nucleic acid or its complement under low stringency conditions,
- (xxvii) "FLJ20342" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions,
- (xxviii) "FLJ20420" (SEQ ID No:128) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20420" encoded by a nucleic acid that hybridizes to the "FLJ20420" nucleic acid or its complement under low stringency conditions,
- (xxix) "FLJ22555" (SEQ ID No:129) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22555" encoded by a nucleic acid that hybridizes to the "FLJ22555" nucleic acid or its complement under low stringency conditions,
- (xxx) "FLJ22678" (SEQ ID No:130) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22678" encoded by a nucleic acid that hybridizes to the "FLJ22678" nucleic acid or its complement under low stringency conditions,
- (xxxi) "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" (SEQ ID No:131) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Galactosylgalactosylxylosylprotein 3-beta-

glucuronosyltransferase 3" encoded by a nucleic acid that hybridizes to the "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" nucleic acid or its complement under low stringency conditions,

(xxxii) "HTRA2" (SEQ ID No:132) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HTRA2" encoded by a nucleic acid that hybridizes to the "HTRA2" nucleic acid or its complement under low stringency conditions,

(xxxiii) "HU-K4 " (SEQ ID No:133) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HU-K4 " encoded by a nucleic acid that hybridizes to the "HU-K4 " nucleic acid or its complement under low stringency conditions,

(xxxiv) "HYPOTHETICAL PROTEIN XP\_174405" (SEQ ID No:134) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN XP\_174405" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN XP\_174405" nucleic acid or its complement under low stringency conditions,

(xxxv) "Hypothetical protein FLJ23356" (SEQ ID No:135) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ23356" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ23356" nucleic acid or its complement under low stringency conditions,

(xxxvi) "Hypothetical protein KIAA0455" (SEQ ID No:136) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0455" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0455" nucleic acid or its complement under low stringency conditions,

(xxxvii) "Hypothetical protein KIAA0971-I" (SEQ ID No:137) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0971-I" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0971-I" nucleic acid or its complement under low stringency conditions,

(xxxviii) "KIAA0062 (FRAGMENT)" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"KIAA0062 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0062 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,  
 (xxxix) "KIAA0090" (SEQ ID No:139) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0090" encoded by a nucleic acid that hybridizes to the "KIAA0090" nucleic acid or its complement under low stringency conditions,

(xl) "KIAA0103" (SEQ ID No:140) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0103" encoded by a nucleic acid that hybridizes to the "KIAA0103" nucleic acid or its complement under low stringency conditions,

(xli) "MGC4248" (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4248" encoded by a nucleic acid that hybridizes to the "MGC4248" nucleic acid or its complement under low stringency conditions,

(xlii) "MGC5442" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions,

(xlili) "NICE-3" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions,

(xliv) "NPC1" (SEQ ID No:144) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPC1" encoded by a nucleic acid that hybridizes to the "NPC1" nucleic acid or its complement under low stringency conditions,

(xlv) "NPD002" (SEQ ID No:145) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPD002" encoded by a nucleic acid that hybridizes to the "NPD002" nucleic acid or its complement under low stringency conditions,

(xlvi) "NPL4, a component of the nuclear pore complex" (SEQ ID No:146) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPL4, a component of the nuclear pore complex"

encoded by a nucleic acid that hybridizes to the "NPL4, a component of the nuclear pore complex" nucleic acid or its complement under low stringency conditions,

(xlvii) "P63 protein" (SEQ ID No:148) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "P63 protein" encoded by a nucleic acid that hybridizes to the "P63 protein" nucleic acid or its complement under low stringency conditions,

(xlviii) "PSMA1" (SEQ ID No:149) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA1" encoded by a nucleic acid that hybridizes to the "PSMA1" nucleic acid or its complement under low stringency conditions,

(xlix) "PSMA3" (SEQ ID No:150) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA3" encoded by a nucleic acid that hybridizes to the "PSMA3" nucleic acid or its complement under low stringency conditions,

(l) "PSMA4" (SEQ ID No:151) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA4" encoded by a nucleic acid that hybridizes to the "PSMA4" nucleic acid or its complement under low stringency conditions,

(li) "PSMA6" (SEQ ID No:152) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA6" encoded by a nucleic acid that hybridizes to the "PSMA6" nucleic acid or its complement under low stringency conditions,

(lii) "PSMB1" (SEQ ID No:153) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB1" encoded by a nucleic acid that hybridizes to the "PSMB1" nucleic acid or its complement under low stringency conditions,

(liii) "PSMB2" (SEQ ID No:154) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB2" encoded by a nucleic acid that hybridizes to the "PSMB2" nucleic acid or its complement under low stringency conditions,

(liv) "PSMB3" (SEQ ID No:155) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB3" encoded by a nucleic acid that hybridizes to the "PSMB3" nucleic acid or its complement under low stringency conditions,

- (lv) "PSMB4" (SEQ ID No:156) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB4" encoded by a nucleic acid that hybridizes to the "PSMB4" nucleic acid or its complement under low stringency conditions,
- (lvi) "PSMB5" (SEQ ID No:157) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB5" encoded by a nucleic acid that hybridizes to the "PSMB5" nucleic acid or its complement under low stringency conditions,
- (lvii) "PSMB6" (SEQ ID No:158) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB6" encoded by a nucleic acid that hybridizes to the "PSMB6" nucleic acid or its complement under low stringency conditions,
- (lviii) "PSMC1" (SEQ ID No:159) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC1" encoded by a nucleic acid that hybridizes to the "PSMC1" nucleic acid or its complement under low stringency conditions,
- (lix) "PSMC2" (SEQ ID No:160) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC2" encoded by a nucleic acid that hybridizes to the "PSMC2" nucleic acid or its complement under low stringency conditions,
- (lx) "PSMC3" (SEQ ID No:161) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC3" encoded by a nucleic acid that hybridizes to the "PSMC3" nucleic acid or its complement under low stringency conditions,
- (lxi) "PSMC4" (SEQ ID No:162) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC4" encoded by a nucleic acid that hybridizes to the "PSMC4" nucleic acid or its complement under low stringency conditions,
- (lxii) "PSMC5" (SEQ ID No:163) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC5" encoded by a nucleic acid that hybridizes to the "PSMC5" nucleic acid or its complement under low stringency conditions,
- (lxiii) "PSMC6" (SEQ ID No:164) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC6"

encoded by a nucleic acid that hybridizes to the "PSMC6" nucleic acid or its complement under low stringency conditions,

(lxiv) "PSMD1" (SEQ ID No:165) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD1" encoded by a nucleic acid that hybridizes to the "PSMD1" nucleic acid or its complement under low stringency conditions,

(lxv) "PSMD11" (SEQ ID No:166) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD11" encoded by a nucleic acid that hybridizes to the "PSMD11" nucleic acid or its complement under low stringency conditions,

(lxvi) "PSMD12" (SEQ ID No:167) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD12" encoded by a nucleic acid that hybridizes to the "PSMD12" nucleic acid or its complement under low stringency conditions,

(lxvii) "PSMD13" (SEQ ID No:168) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD13" encoded by a nucleic acid that hybridizes to the "PSMD13" nucleic acid or its complement under low stringency conditions,

(lxviii) "PSMD2" (SEQ ID No:169) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD2" encoded by a nucleic acid that hybridizes to the "PSMD2" nucleic acid or its complement under low stringency conditions,

(lxix) "PSMD3" (SEQ ID No:170) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD3" encoded by a nucleic acid that hybridizes to the "PSMD3" nucleic acid or its complement under low stringency conditions,

(lxx) "PSMD4" (SEQ ID No:171) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD4" encoded by a nucleic acid that hybridizes to the "PSMD4" nucleic acid or its complement under low stringency conditions,

(lxxi) "Prohibitin" (SEQ ID No:173) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Prohibitin" encoded by a nucleic acid that hybridizes to the "Prohibitin" nucleic acid or its complement under low stringency conditions,

(lxxii) "RPS6KA3" (SEQ ID No:174) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RPS6KA3" encoded by a nucleic acid that hybridizes to the "RPS6KA3" nucleic acid or its complement under low stringency conditions,

(lxxiii) "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" (SEQ ID No:175) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" encoded by a nucleic acid that hybridizes to the "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" nucleic acid or its complement under low stringency conditions,

(lxxiv) "STRA6 isoform 1" (SEQ ID No:176) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STRA6 isoform 1" encoded by a nucleic acid that hybridizes to the "STRA6 isoform 1" nucleic acid or its complement under low stringency conditions,

(lxxv) "Serine/threonine protein phosphatase 6" (SEQ ID No:90) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Serine/threonine protein phosphatase 6" encoded by a nucleic acid that hybridizes to the "Serine/threonine protein phosphatase 6" nucleic acid or its complement under low stringency conditions,

(lxxvi) "Sortilin 1" (SEQ ID No:177) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sortilin 1" encoded by a nucleic acid that hybridizes to the "Sortilin 1" nucleic acid or its complement under low stringency conditions,

(lxxvii) "Stearoyl-CoA desaturase" (SEQ ID No:178) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Stearoyl-CoA desaturase" encoded by a nucleic acid that hybridizes to the "Stearoyl-CoA desaturase" nucleic acid or its complement under low stringency conditions,

(lxxviii) "Tparl" (SEQ ID No:179) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Tparl" encoded by a nucleic acid that hybridizes to the "Tparl" nucleic acid or its complement under low stringency conditions,

(lxxix) "Ubiquitin-protein ligase EDD" (SEQ ID No:180) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"Ubiquitin-protein ligase EDD" encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase EDD" nucleic acid or its complement under low stringency conditions, (lxxx) "Voltage-dependent anion channel 2" (SEQ ID No:181) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Voltage-dependent anion channel 2" encoded by a nucleic acid that hybridizes to the "Voltage-dependent anion channel 2" nucleic acid or its complement under low stringency conditions,

(lxxxi) "Wolframin" (SEQ ID No:182) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Wolframin" encoded by a nucleic acid that hybridizes to the "Wolframin" nucleic acid or its complement under low stringency conditions,

(lxxxii) "cholinergic receptor, nicotinic, alpha polypeptide 3" (SEQ ID No:183) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "cholinergic receptor, nicotinic, alpha polypeptide 3" encoded by a nucleic acid that hybridizes to the "cholinergic receptor, nicotinic, alpha polypeptide 3" nucleic acid or its complement under low stringency conditions, and

(lxxxiii) "ensp00000297280 (hypothetical protein with p-loop)" (SEQ ID No:184) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ensp00000297280 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ensp00000297280 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions, and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

2. The protein complex according to No. 1 wherein the first protein is the protein "Presenilin-2" (SEQ ID NO. 172), or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of 'Presenilin-2'



encoded by a nucleic acid that hybridizes to the 'Presenilin-2' under low stringency conditions.

3. The protein complex according to No. 1 selected from complex (I) and comprising the following proteins:

- (i) "18 kDa microsomal signal peptidase subunit" (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "18 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,
- (ii) "200 kDa proteasome activator" (SEQ ID No:101) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "200 kDa proteasome activator" encoded by a nucleic acid that hybridizes to the "200 kDa proteasome activator" nucleic acid or its complement under low stringency conditions,
- (iii) "ABCB11" (SEQ ID No:102) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ABCB11" encoded by a nucleic acid that hybridizes to the "ABCB11" nucleic acid or its complement under low stringency conditions,
- (iv) "ATM" (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATM" encoded by a nucleic acid that hybridizes to the "ATM" nucleic acid or its complement under low stringency conditions,
- (v) "ATP-binding cassette protein, sub-family B, member 1" (SEQ ID No:104) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette protein, sub-family B, member 1" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette protein, sub-family B, member 1" nucleic acid or its complement under low stringency conditions,
- (vi) "ATP-dependent metalloprotease FtsH1 homolog" (SEQ ID No:105) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-dependent metalloprotease FtsH1 homolog" encoded by a nucleic acid that hybridizes to the "ATP-dependent metalloprotease FtsH1 homolog" nucleic acid or its complement under low stringency conditions,

- (vii) "ATP7A" (SEQ ID No:106) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP7A" encoded by a nucleic acid that hybridizes to the "ATP7A" nucleic acid or its complement under low stringency conditions,
- (viii) "Acetolactate synthase homolog" (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Acetolactate synthase homolog" encoded by a nucleic acid that hybridizes to the "Acetolactate synthase homolog" nucleic acid or its complement under low stringency conditions,
- (ix) "Adrenoleukodystrophy protein" (SEQ ID No:108) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Adrenoleukodystrophy protein" encoded by a nucleic acid that hybridizes to the "Adrenoleukodystrophy protein" nucleic acid or its complement under low stringency conditions,
- (x) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,
- (xi) "BIG1" (SEQ ID No:110) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BIG1" encoded by a nucleic acid that hybridizes to the "BIG1" nucleic acid or its complement under low stringency conditions,
- (xii) "BTAF1" (SEQ ID No:111) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BTAF1" encoded by a nucleic acid that hybridizes to the "BTAF1" nucleic acid or its complement under low stringency conditions,
- (xiii) "CD97" (SEQ ID No:112) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CD97" encoded by a nucleic acid that hybridizes to the "CD97" nucleic acid or its complement under low stringency conditions,
- (xiv) "CDM\_HUMAN" (SEQ ID No:113) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDM\_HUMAN" encoded by a nucleic acid that hybridizes to the "CDM\_HUMAN" nucleic acid or its complement under low stringency conditions,

(xv) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,

(xvi) "CGI-51" (SEQ ID No:115) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-51" encoded by a nucleic acid that hybridizes to the "CGI-51" nucleic acid or its complement under low stringency conditions,

(xvii) "CHRNA3" (SEQ ID No:116) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CHRNA3" encoded by a nucleic acid that hybridizes to the "CHRNA3" nucleic acid or its complement under low stringency conditions,

(xviii) "Calcium-binding protein P22" (SEQ ID No:117) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calcium-binding protein P22" encoded by a nucleic acid that hybridizes to the "Calcium-binding protein P22" nucleic acid or its complement under low stringency conditions,

(xix) "Cation-chloride cotransporter-interacting protein" (SEQ ID No:118) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cation-chloride cotransporter-interacting protein" encoded by a nucleic acid that hybridizes to the "Cation-chloride cotransporter-interacting protein" nucleic acid or its complement under low stringency conditions,

(xx) "Centromere/kinetochore protein ZW10 homolog" (SEQ ID No:119) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Centromere/kinetochore protein ZW10 homolog" encoded by a nucleic acid that hybridizes to the "Centromere/kinetochore protein ZW10 homolog" nucleic acid or its complement under low stringency conditions,

(xxi) "Cerebral protein 10" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cerebral protein 10" encoded by a nucleic acid that hybridizes to the "Cerebral protein 10" nucleic acid or its complement under low stringency conditions,

(xxii) "DAAM1" (SEQ ID No:121) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DAAM1" encoded by a nucleic acid that hybridizes to the "DAAM1" nucleic acid or its complement under low stringency conditions,

- (xxiii) "DAPK1" (SEQ ID No:122) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DAPK1" encoded by a nucleic acid that hybridizes to the "DAPK1" nucleic acid or its complement under low stringency conditions,
- (xxiv) "DKFZp586c1924" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DKFZp586c1924" encoded by a nucleic acid that hybridizes to the "DKFZp586c1924" nucleic acid or its complement under low stringency conditions,
- (xxv) "DOCK3" (SEQ ID No:123) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DOCK3" encoded by a nucleic acid that hybridizes to the "DOCK3" nucleic acid or its complement under low stringency conditions,
- (xxvi) "Down syndrome critical region protein 2" (SEQ ID No:124) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Down syndrome critical region protein 2" encoded by a nucleic acid that hybridizes to the "Down syndrome critical region protein 2" nucleic acid or its complement under low stringency conditions,
- (xxvii) "ECSIT" (SEQ ID No:125) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ECSIT" encoded by a nucleic acid that hybridizes to the "ECSIT" nucleic acid or its complement under low stringency conditions,
- (xxviii) "FACL1" (SEQ ID No:126) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FACL1" encoded by a nucleic acid that hybridizes to the "FACL1" nucleic acid or its complement under low stringency conditions,
- (xxix) "FLJ20342" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions,
- (xxx) "FLJ20420" (SEQ ID No:128) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20420" encoded by a nucleic acid that hybridizes to the "FLJ20420" nucleic acid or its complement under low stringency conditions,

(xxxi) "FLJ22555" (SEQ ID No:129) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22555" encoded by a nucleic acid that hybridizes to the "FLJ22555" nucleic acid or its complement under low stringency conditions,

(xxxii) "FLJ22678" (SEQ ID No:130) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22678" encoded by a nucleic acid that hybridizes to the "FLJ22678" nucleic acid or its complement under low stringency conditions,

(xxxiii) "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" (SEQ ID No:131) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" encoded by a nucleic acid that hybridizes to the "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" nucleic acid or its complement under low stringency conditions,

(xxxiv) "HTRA2" (SEQ ID No:132) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HTRA2" encoded by a nucleic acid that hybridizes to the "HTRA2" nucleic acid or its complement under low stringency conditions,

(xxxv) "HU-K4 " (SEQ ID No:133) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HU-K4 " encoded by a nucleic acid that hybridizes to the "HU-K4 " nucleic acid or its complement under low stringency conditions,

(xxxvi) "HYPOTHETICAL PROTEIN XP\_174405" (SEQ ID No:134) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN XP\_174405" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN XP\_174405" nucleic acid or its complement under low stringency conditions,

(xxxvii) "Hypothetical protein FLJ23356" (SEQ ID No:135) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ23356" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ23356" nucleic acid or its complement under low stringency conditions,

(xxxviii) "Hypothetical protein KIAA0455" (SEQ ID No:136) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a

variant of "Hypothetical protein KIAA0455" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0455" nucleic acid or its complement under low stringency conditions,

(xxxix) "Hypothetical protein KIAA0971-I" (SEQ ID No:137) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0971-I" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0971-I" nucleic acid or its complement under low stringency conditions,

(xl) "KIAA0062 (FRAGMENT)" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0062 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0062 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xli) "KIAA0090" (SEQ ID No:139) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0090" encoded by a nucleic acid that hybridizes to the "KIAA0090" nucleic acid or its complement under low stringency conditions,

(xlii) "KIAA0103" (SEQ ID No:140) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0103" encoded by a nucleic acid that hybridizes to the "KIAA0103" nucleic acid or its complement under low stringency conditions,

(xliii) "MGC4248" (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4248" encoded by a nucleic acid that hybridizes to the "MGC4248" nucleic acid or its complement under low stringency conditions,

(xliv) "MGC5442" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions,

(xlv) "NICE-3" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions,

(xlvi) "NPC1" (SEQ ID No:144) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPC1" encoded by a

nucleic acid that hybridizes to the "NPC1" nucleic acid or its complement under low stringency conditions,

(xlvii) "NPD002" (SEQ ID No:145) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPD002" encoded by a nucleic acid that hybridizes to the "NPD002" nucleic acid or its complement under low stringency conditions,

(xlviii) "NPL4, a component of the nuclear pore complex" (SEQ ID No:146) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPL4, a component of the nuclear pore complex" encoded by a nucleic acid that hybridizes to the "NPL4, a component of the nuclear pore complex" nucleic acid or its complement under low stringency conditions,

(xlix) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,

(l) "P63 protein" (SEQ ID No:148) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "P63 protein" encoded by a nucleic acid that hybridizes to the "P63 protein" nucleic acid or its complement under low stringency conditions,

(li) "PSMA1" (SEQ ID No:149) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA1" encoded by a nucleic acid that hybridizes to the "PSMA1" nucleic acid or its complement under low stringency conditions,

(lii) "PSMA3" (SEQ ID No:150) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA3" encoded by a nucleic acid that hybridizes to the "PSMA3" nucleic acid or its complement under low stringency conditions,

(liii) "PSMA4" (SEQ ID No:151) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA4" encoded by a nucleic acid that hybridizes to the "PSMA4" nucleic acid or its complement under low stringency conditions,

(liv) "PSMA6" (SEQ ID No:152) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA6"

encoded by a nucleic acid that hybridizes to the "PSMA6" nucleic acid or its complement under low stringency conditions,

(lv) "PSMB1" (SEQ ID No:153) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB1" encoded by a nucleic acid that hybridizes to the "PSMB1" nucleic acid or its complement under low stringency conditions,

(lvi) "PSMB2" (SEQ ID No:154) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB2" encoded by a nucleic acid that hybridizes to the "PSMB2" nucleic acid or its complement under low stringency conditions,

(lvii) "PSMB3" (SEQ ID No:155) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB3" encoded by a nucleic acid that hybridizes to the "PSMB3" nucleic acid or its complement under low stringency conditions,

(lviii) "PSMB4" (SEQ ID No:156) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB4" encoded by a nucleic acid that hybridizes to the "PSMB4" nucleic acid or its complement under low stringency conditions,

(lix) "PSMB5" (SEQ ID No:157) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB5" encoded by a nucleic acid that hybridizes to the "PSMB5" nucleic acid or its complement under low stringency conditions,

(lx) "PSMB6" (SEQ ID No:158) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB6" encoded by a nucleic acid that hybridizes to the "PSMB6" nucleic acid or its complement under low stringency conditions,

(lxi) "PSMC1" (SEQ ID No:159) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC1" encoded by a nucleic acid that hybridizes to the "PSMC1" nucleic acid or its complement under low stringency conditions,

(lxii) "PSMC2" (SEQ ID No:160) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC2" encoded by a nucleic acid that hybridizes to the "PSMC2" nucleic acid or its complement under low stringency conditions,



- (Ixm) "PSMC3" (SEQ ID No:161) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC3" encoded by a nucleic acid that hybridizes to the "PSMC3" nucleic acid or its complement under low stringency conditions,
- (Ixiii) "PSMC4" (SEQ ID No:162) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC4" encoded by a nucleic acid that hybridizes to the "PSMC4" nucleic acid or its complement under low stringency conditions,
- (Ixiv) "PSMC5" (SEQ ID No:163) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC5" encoded by a nucleic acid that hybridizes to the "PSMC5" nucleic acid or its complement under low stringency conditions,
- (Ixv) "PSMC6" (SEQ ID No:164) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC6" encoded by a nucleic acid that hybridizes to the "PSMC6" nucleic acid or its complement under low stringency conditions,
- (Ixvi) "PSMD1" (SEQ ID No:165) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD1" encoded by a nucleic acid that hybridizes to the "PSMD1" nucleic acid or its complement under low stringency conditions,
- (Ixvii) "PSMD11" (SEQ ID No:166) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD11" encoded by a nucleic acid that hybridizes to the "PSMD11" nucleic acid or its complement under low stringency conditions,
- (Ixviii) "PSMD12" (SEQ ID No:167) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD12" encoded by a nucleic acid that hybridizes to the "PSMD12" nucleic acid or its complement under low stringency conditions,
- (Ixix) "PSMD13" (SEQ ID No:168) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD13" encoded by a nucleic acid that hybridizes to the "PSMD13" nucleic acid or its complement under low stringency conditions,
- (Ixx) "PSMD2" (SEQ ID No:169) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD2"

encoded by a nucleic acid that hybridizes to the "PSMD2" nucleic acid or its complement under low stringency conditions,

(lxxii) "PSMD3" (SEQ ID No:170) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD3" encoded by a nucleic acid that hybridizes to the "PSMD3" nucleic acid or its complement under low stringency conditions,

(lxxiii) "PSMD4" (SEQ ID No:171) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD4" encoded by a nucleic acid that hybridizes to the "PSMD4" nucleic acid or its complement under low stringency conditions,

(lxxiv) "Presenilin 2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions,

(lxxv) "Prohibitin" (SEQ ID No:173) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Prohibitin" encoded by a nucleic acid that hybridizes to the "Prohibitin" nucleic acid or its complement under low stringency conditions,

(lxxvi) "RPS6KA3" (SEQ ID No:174) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RPS6KA3" encoded by a nucleic acid that hybridizes to the "RPS6KA3" nucleic acid or its complement under low stringency conditions,

(lxxvii) "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" (SEQ ID No:175) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" encoded by a nucleic acid that hybridizes to the "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" nucleic acid or its complement under low stringency conditions,

(lxxviii) "STRA6 isoform 1" (SEQ ID No:176) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STRA6 isoform 1" encoded by a nucleic acid that hybridizes to the "STRA6 isoform 1" nucleic acid or its complement under low stringency conditions,

(lxxix) "Serine/threonine protein phosphatase 6" (SEQ ID No:90) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a

variant of "Serine/threonine protein phosphatase 6" encoded by a nucleic acid that hybridizes to the "Serine/threonine protein phosphatase 6" nucleic acid or its complement under low stringency conditions,

(lxxx) "Sortilin 1" (SEQ ID No:177) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sortilin 1" encoded by a nucleic acid that hybridizes to the "Sortilin 1" nucleic acid or its complement under low stringency conditions,

(lxxxi) "Stearoyl-CoA desaturase" (SEQ ID No:178) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Stearoyl-CoA desaturase" encoded by a nucleic acid that hybridizes to the "Stearoyl-CoA desaturase" nucleic acid or its complement under low stringency conditions,

(lxxxii) "Tparl" (SEQ ID No:179) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Tparl" encoded by a nucleic acid that hybridizes to the "Tparl" nucleic acid or its complement under low stringency conditions,

(lxxxiii) "Ubiquitin-protein ligase EDD" (SEQ ID No:180) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Ubiquitin-protein ligase EDD" encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase EDD" nucleic acid or its complement under low stringency conditions,

(lxxxiv) "Voltage-dependent anion channel 2" (SEQ ID No:181) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Voltage-dependent anion channel 2" encoded by a nucleic acid that hybridizes to the "Voltage-dependent anion channel 2" nucleic acid or its complement under low stringency conditions,

(lxxxv) "Wolframin" (SEQ ID No:182) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Wolframin" encoded by a nucleic acid that hybridizes to the "Wolframin" nucleic acid or its complement under low stringency conditions,

(lxxxvi) "cholinergic receptor, nicotinic, alpha polypeptide 3" (SEQ ID No:183) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "cholinergic receptor, nicotinic, alpha polypeptide 3" encoded by a nucleic acid that hybridizes to the "cholinergic receptor, nicotinic, alpha polypeptide 3" nucleic acid or its complement under low stringency conditions, and/or

(lxxxvii) "ensp00000297280 (hypothetical protein with p-loop)" (SEQ ID No:184) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ensp00000297280 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ensp00000297280 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions.

4. The protein complex according to No. 1 comprising all but 1 - 82 of the following proteins:

- (i) "18 kDa microsomal signal peptidase subunit" (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "18 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,
- (ii) "200 kDa proteasome activator" (SEQ ID No:101) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "200 kDa proteasome activator" encoded by a nucleic acid that hybridizes to the "200 kDa proteasome activator" nucleic acid or its complement under low stringency conditions,
- (iii) "ABCB11" (SEQ ID No:102) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ABCB11" encoded by a nucleic acid that hybridizes to the "ABCB11" nucleic acid or its complement under low stringency conditions,
- (iv) "ATM" (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATM" encoded by a nucleic acid that hybridizes to the "ATM" nucleic acid or its complement under low stringency conditions,
- (v) "ATP-binding cassette protein, sub-family B, member 1" (SEQ ID No:104) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette protein, sub-family B, member 1" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette protein, sub-family B, member 1" nucleic acid or its complement under low stringency conditions,
- (vi) "ATP-dependent metalloprotease FtsH1 homolog" (SEQ ID No:105) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-dependent metalloprotease FtsH1 homolog" encoded by a nucleic

acid that hybridizes to the "ATP-dependent metalloprotease FtsH1 homolog" nucleic acid or its complement under low stringency conditions,

(vii) "ATP7A" (SEQ ID No:106) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP7A" encoded by a nucleic acid that hybridizes to the "ATP7A" nucleic acid or its complement under low stringency conditions,

(viii) "Acetolactate synthase homolog" (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Acetolactate synthase homolog" encoded by a nucleic acid that hybridizes to the "Acetolactate synthase homolog" nucleic acid or its complement under low stringency conditions,

(ix) "Adrenoleukodystrophy protein" (SEQ ID No:108) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Adrenoleukodystrophy protein" encoded by a nucleic acid that hybridizes to the "Adrenoleukodystrophy protein" nucleic acid or its complement under low stringency conditions,

(x) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,

(xi) "BIG1" (SEQ ID No:110) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BIG1" encoded by a nucleic acid that hybridizes to the "BIG1" nucleic acid or its complement under low stringency conditions,

(xii) "BTAF1" (SEQ ID No:111) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BTAF1" encoded by a nucleic acid that hybridizes to the "BTAF1" nucleic acid or its complement under low stringency conditions,

(xiii) "CD97" (SEQ ID No:112) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CD97" encoded by a nucleic acid that hybridizes to the "CD97" nucleic acid or its complement under low stringency conditions,

(xiv) "CDM\_HUMAN" (SEQ ID No:113) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"CDM\_HUMAN" encoded by a nucleic acid that hybridizes to the "CDM\_HUMAN" nucleic acid or its complement under low stringency conditions,

(xv) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,

(xvi) "CGI-51" (SEQ ID No:115) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-51" encoded by a nucleic acid that hybridizes to the "CGI-51" nucleic acid or its complement under low stringency conditions,

(xvii) "CHRNA3" (SEQ ID No:116) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CHRNA3" encoded by a nucleic acid that hybridizes to the "CHRNA3" nucleic acid or its complement under low stringency conditions,

(xviii) "Calcium-binding protein P22" (SEQ ID No:117) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calcium-binding protein P22" encoded by a nucleic acid that hybridizes to the "Calcium-binding protein P22" nucleic acid or its complement under low stringency conditions,

(xix) "Cation-chloride cotransporter-interacting protein" (SEQ ID No:118) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cation-chloride cotransporter-interacting protein" encoded by a nucleic acid that hybridizes to the "Cation-chloride cotransporter-interacting protein" nucleic acid or its complement under low stringency conditions,

(xx) "Centromere/kinetochore protein ZW10 homolog" (SEQ ID No:119) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Centromere/kinetochore protein ZW10 homolog" encoded by a nucleic acid that hybridizes to the "Centromere/kinetochore protein ZW10 homolog" nucleic acid or its complement under low stringency conditions,

(xxi) "Cerebral protein 10" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cerebral protein 10" encoded by a nucleic acid that hybridizes to the "Cerebral protein 10" nucleic acid or its complement under low stringency conditions,

(xxii) "DAAM1" (SEQ ID No:121) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DAAM1"

encoded by a nucleic acid that hybridizes to the "DAAM1" nucleic acid or its complement under low stringency conditions,

(xxiii) "DAPK1" (SEQ ID No:122) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DAPK1" encoded by a nucleic acid that hybridizes to the "DAPK1" nucleic acid or its complement under low stringency conditions,

(xxiv) "DKFZp586c1924" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DKFZp586c1924" encoded by a nucleic acid that hybridizes to the "DKFZp586c1924" nucleic acid or its complement under low stringency conditions,

(xxv) "DOCK3" (SEQ ID No:123) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DOCK3" encoded by a nucleic acid that hybridizes to the "DOCK3" nucleic acid or its complement under low stringency conditions,

(xxvi) "Down syndrome critical region protein 2" (SEQ ID No:124) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Down syndrome critical region protein 2" encoded by a nucleic acid that hybridizes to the "Down syndrome critical region protein 2" nucleic acid or its complement under low stringency conditions,

(xxvii) "ECSIT" (SEQ ID No:125) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ECSIT" encoded by a nucleic acid that hybridizes to the "ECSIT" nucleic acid or its complement under low stringency conditions,

(xxviii) "FACL1" (SEQ ID No:126) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FACL1" encoded by a nucleic acid that hybridizes to the "FACL1" nucleic acid or its complement under low stringency conditions,

(xxix) "FLJ20342" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions,

(xxx) "FLJ20420" (SEQ ID No:128) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20420"

encoded by a nucleic acid that hybridizes to the "FLJ20420" nucleic acid or its complement under low stringency conditions,

(xxxi) "FLJ22555" (SEQ ID No:129) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22555" encoded by a nucleic acid that hybridizes to the "FLJ22555" nucleic acid or its complement under low stringency conditions,

(xxxii) "FLJ22678" (SEQ ID No:130) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22678" encoded by a nucleic acid that hybridizes to the "FLJ22678" nucleic acid or its complement under low stringency conditions,

(xxxiii) "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" (SEQ ID No:131) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" encoded by a nucleic acid that hybridizes to the "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" nucleic acid or its complement under low stringency conditions,

(xxxiv) "HTRA2" (SEQ ID No:132) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HTRA2" encoded by a nucleic acid that hybridizes to the "HTRA2" nucleic acid or its complement under low stringency conditions,

(xxxv) "HU-K4 " (SEQ ID No:133) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HU-K4 " encoded by a nucleic acid that hybridizes to the "HU-K4 " nucleic acid or its complement under low stringency conditions,

(xxxvi) "HYPOTHETICAL PROTEIN XP\_174405" (SEQ ID No:134) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN XP\_174405" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN XP\_174405" nucleic acid or its complement under low stringency conditions,

(xxxvii) "Hypothetical protein FLJ23356" (SEQ ID No:135) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ23356" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ23356" nucleic acid or its complement under low stringency conditions,



(xxxviii) "Hypothetical protein KIAA0455" (SEQ ID No:136) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0455" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0455" nucleic acid or its complement under low stringency conditions,

(xxxix) "Hypothetical protein KIAA0971-I" (SEQ ID No:137) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0971-I" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0971-I" nucleic acid or its complement under low stringency conditions,

(xl) "KIAA0062 (FRAGMENT)" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0062 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0062 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xli) "KIAA0090" (SEQ ID No:139) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0090" encoded by a nucleic acid that hybridizes to the "KIAA0090" nucleic acid or its complement under low stringency conditions,

(xlii) "KIAA0103" (SEQ ID No:140) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0103" encoded by a nucleic acid that hybridizes to the "KIAA0103" nucleic acid or its complement under low stringency conditions,

(xliii) "MGC4248" (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4248" encoded by a nucleic acid that hybridizes to the "MGC4248" nucleic acid or its complement under low stringency conditions,

(xliv) "MGC5442" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions,

(xlv) "NICE-3" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions,

(xlv) "NPC1" (SEQ ID No:144) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPC1" encoded by a nucleic acid that hybridizes to the "NPC1" nucleic acid or its complement under low stringency conditions,

(xlvii) "NPD002" (SEQ ID No:145) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPD002" encoded by a nucleic acid that hybridizes to the "NPD002" nucleic acid or its complement under low stringency conditions,

(xlviii) "NPL4, a component of the nuclear pore complex" (SEQ ID No:146) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPL4, a component of the nuclear pore complex" encoded by a nucleic acid that hybridizes to the "NPL4, a component of the nuclear pore complex" nucleic acid or its complement under low stringency conditions,

(xlix) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,

(l) "P63 protein" (SEQ ID No:148) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "P63 protein" encoded by a nucleic acid that hybridizes to the "P63 protein" nucleic acid or its complement under low stringency conditions,

(li) "PSMA1" (SEQ ID No:149) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA1" encoded by a nucleic acid that hybridizes to the "PSMA1" nucleic acid or its complement under low stringency conditions,

(lii) "PSMA3" (SEQ ID No:150) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA3" encoded by a nucleic acid that hybridizes to the "PSMA3" nucleic acid or its complement under low stringency conditions,

(liii) "PSMA4" (SEQ ID No:151) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA4" encoded by a nucleic acid that hybridizes to the "PSMA4" nucleic acid or its complement under low stringency conditions,

- (liv) "PSMA6" (SEQ ID No:152) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA6" encoded by a nucleic acid that hybridizes to the "PSMA6" nucleic acid or its complement under low stringency conditions,
- (lv) "PSMB1" (SEQ ID No:153) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB1" encoded by a nucleic acid that hybridizes to the "PSMB1" nucleic acid or its complement under low stringency conditions,
- (lvi) "PSMB2" (SEQ ID No:154) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB2" encoded by a nucleic acid that hybridizes to the "PSMB2" nucleic acid or its complement under low stringency conditions,
- (lvii) "PSMB3" (SEQ ID No:155) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB3" encoded by a nucleic acid that hybridizes to the "PSMB3" nucleic acid or its complement under low stringency conditions,
- (lviii) "PSMB4" (SEQ ID No:156) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB4" encoded by a nucleic acid that hybridizes to the "PSMB4" nucleic acid or its complement under low stringency conditions,
- (lix) "PSMB5" (SEQ ID No:157) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB5" encoded by a nucleic acid that hybridizes to the "PSMB5" nucleic acid or its complement under low stringency conditions,
- (lx) "PSMB6" (SEQ ID No:158) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB6" encoded by a nucleic acid that hybridizes to the "PSMB6" nucleic acid or its complement under low stringency conditions,
- (lxi) "PSMC1" (SEQ ID No:159) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC1" encoded by a nucleic acid that hybridizes to the "PSMC1" nucleic acid or its complement under low stringency conditions,
- (lxii) "PSMC2" (SEQ ID No:160) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC2"

encoded by a nucleic acid that hybridizes to the "PSMC2" nucleic acid or its complement under low stringency conditions,

(lxiii) "PSMC3" (SEQ ID No:161) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC3" encoded by a nucleic acid that hybridizes to the "PSMC3" nucleic acid or its complement under low stringency conditions,

(lxiv) "PSMC4" (SEQ ID No:162) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC4" encoded by a nucleic acid that hybridizes to the "PSMC4" nucleic acid or its complement under low stringency conditions,

(lxv) "PSMC5" (SEQ ID No:163) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC5" encoded by a nucleic acid that hybridizes to the "PSMC5" nucleic acid or its complement under low stringency conditions,

(lxvi) "PSMC6" (SEQ ID No:164) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC6" encoded by a nucleic acid that hybridizes to the "PSMC6" nucleic acid or its complement under low stringency conditions,

(lxvii) "PSMD1" (SEQ ID No:165) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD1" encoded by a nucleic acid that hybridizes to the "PSMD1" nucleic acid or its complement under low stringency conditions,

(lxviii) "PSMD11" (SEQ ID No:166) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD11" encoded by a nucleic acid that hybridizes to the "PSMD11" nucleic acid or its complement under low stringency conditions,

(lxix) "PSMD12" (SEQ ID No:167) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD12" encoded by a nucleic acid that hybridizes to the "PSMD12" nucleic acid or its complement under low stringency conditions,

(lxx) "PSMD13" (SEQ ID No:168) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD13" encoded by a nucleic acid that hybridizes to the "PSMD13" nucleic acid or its complement under low stringency conditions,

(lxxi) "PSMD2" (SEQ ID No:169) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD2" encoded by a nucleic acid that hybridizes to the "PSMD2" nucleic acid or its complement under low stringency conditions,

(lxxii) "PSMD3" (SEQ ID No:170) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD3" encoded by a nucleic acid that hybridizes to the "PSMD3" nucleic acid or its complement under low stringency conditions,

(lxxiii) "PSMD4" (SEQ ID No:171) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD4" encoded by a nucleic acid that hybridizes to the "PSMD4" nucleic acid or its complement under low stringency conditions,

(lxxiv) "Presenilin 2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions,

(lxxv) "Prohibitin" (SEQ ID No:173) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Prohibitin" encoded by a nucleic acid that hybridizes to the "Prohibitin" nucleic acid or its complement under low stringency conditions,

(lxxvi) "RPS6KA3" (SEQ ID No:174) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RPS6KA3" encoded by a nucleic acid that hybridizes to the "RPS6KA3" nucleic acid or its complement under low stringency conditions,

(lxxvii) "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" (SEQ ID No:175) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" encoded by a nucleic acid that hybridizes to the "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" nucleic acid or its complement under low stringency conditions,

(lxxviii) "STRA6 isoform 1" (SEQ ID No:176) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STRA6 isoform 1" encoded by a nucleic acid that hybridizes to the "STRA6 isoform 1" nucleic acid or its complement under low stringency conditions,

(lxxix) "Serine/threonine protein phosphatase 6" (SEQ ID No:90) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Serine/threonine protein phosphatase 6" encoded by a nucleic acid that hybridizes to the "Serine/threonine protein phosphatase 6" nucleic acid or its complement under low stringency conditions,

(lxxx) "Sortilin 1" (SEQ ID No:177) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sortilin 1" encoded by a nucleic acid that hybridizes to the "Sortilin 1" nucleic acid or its complement under low stringency conditions,

(lxxxi) "Stearoyl-CoA desaturase" (SEQ ID No:178) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Stearoyl-CoA desaturase" encoded by a nucleic acid that hybridizes to the "Stearoyl-CoA desaturase" nucleic acid or its complement under low stringency conditions,

(lxxxii) "Tparl" (SEQ ID No:179) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Tparl" encoded by a nucleic acid that hybridizes to the "Tparl" nucleic acid or its complement under low stringency conditions,

(lxxxiii) "Ubiquitin-protein ligase EDD" (SEQ ID No:180) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Ubiquitin-protein ligase EDD" encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase EDD" nucleic acid or its complement under low stringency conditions,

(lxxxiv) "Voltage-dependent anion channel 2" (SEQ ID No:181) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Voltage-dependent anion channel 2" encoded by a nucleic acid that hybridizes to the "Voltage-dependent anion channel 2" nucleic acid or its complement under low stringency conditions,

(lxxxv) "Wolframin" (SEQ ID No:182) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Wolframin" encoded by a nucleic acid that hybridizes to the "Wolframin" nucleic acid or its complement under low stringency conditions,

(lxxxvi) "cholinergic receptor, nicotinic, alpha polypeptide 3" (SEQ ID No:183) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "cholinergic receptor, nicotinic, alpha polypeptide 3"

encoded by a nucleic acid that hybridizes to the "cholinergic receptor, nicotinic, alpha polypeptide 3" nucleic acid or its complement under low stringency conditions, (lxxxvii) "ensp00000297280 (hypothetical protein with p-loop)" (SEQ ID No:184) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ensp00000297280 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ensp00000297280 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions.

5. The complex of any of No. 1 - 4 comprising a functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein, respectively.

6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.

7. The complex of any of No. 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.

8. The complex of any of No. 1 - 7 that is involved in the the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)).

9. A process for preparing a complex of any of No. 1 - 8 and optionally the components thereof comprising the following steps: expressing a protein (bait) of the complex, preferably a tagged protein, in a target cell, isolating the protein complex which is attached to the bait protein, and optionally dissociating the protein complex and isolating the individual complex members.

10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.

11. The process according to any of No. 9 - 10 wherein the two tags are separated by a cleavage site for a protease.

12. Component of the Presenilin 2 complex obtainable by a process according to any of No. 9 - 11.

13. Protein of the Presenilin 2 complex selected from

(i) "CDM\_HUMAN" (SEQ ID No:113) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDM\_HUMAN" encoded by a nucleic acid that hybridizes to the "CDM\_HUMAN" nucleic acid or its complement under low stringency conditions,

(ii) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,

(iii) "CGI-51" (SEQ ID No:115) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-51" encoded by a nucleic acid that hybridizes to the "CGI-51" nucleic acid or its complement under low stringency conditions,

(iv) "Cerebral protein 10" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cerebral protein 10" encoded by a nucleic acid that hybridizes to the "Cerebral protein 10" nucleic acid or its complement under low stringency conditions,



- (v) "DKFZp586c1924" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DKFZp586c1924" encoded by a nucleic acid that hybridizes to the "DKFZp586c1924" nucleic acid or its complement under low stringency conditions,
- (vi) "FLJ20342" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions,
- (vii) "FLJ20420" (SEQ ID No:128) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20420" encoded by a nucleic acid that hybridizes to the "FLJ20420" nucleic acid or its complement under low stringency conditions,
- (viii) "FLJ22555" (SEQ ID No:129) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22555" encoded by a nucleic acid that hybridizes to the "FLJ22555" nucleic acid or its complement under low stringency conditions,
- (ix) "FLJ22678" (SEQ ID No:130) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22678" encoded by a nucleic acid that hybridizes to the "FLJ22678" nucleic acid or its complement under low stringency conditions,
- (x) "HYPOTHETICAL PROTEIN XP\_174405" (SEQ ID No:134) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN XP\_174405" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN XP\_174405" nucleic acid or its complement under low stringency conditions,
- (xi) "Hypothetical protein FLJ23356" (SEQ ID No:135) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ23356" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ23356" nucleic acid or its complement under low stringency conditions,
- (xii) "Hypothetical protein KIAA0455" (SEQ ID No:136) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0455" encoded by a nucleic acid that hybridizes to the

"Hypothetical protein KIAA0455" nucleic acid or its complement under low stringency conditions,

(xiii) "Hypothetical protein KIAA0971-I" (SEQ ID No:137) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0971-I" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0971-I" nucleic acid or its complement under low stringency conditions,

(xiv) "KIAA0062 (FRAGMENT)" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0062 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0062 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xv) "KIAA0090" (SEQ ID No:139) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0090" encoded by a nucleic acid that hybridizes to the "KIAA0090" nucleic acid or its complement under low stringency conditions,

(xvi) "KIAA0103" (SEQ ID No:140) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0103" encoded by a nucleic acid that hybridizes to the "KIAA0103" nucleic acid or its complement under low stringency conditions,

(xvii) "MGC4248" (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4248" encoded by a nucleic acid that hybridizes to the "MGC4248" nucleic acid or its complement under low stringency conditions,

(xviii) "MGC5442" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions,

(xix) "NICE-3" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions,

(xx) "NPL4, a component of the nuclear pore complex" (SEQ ID No:146) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPL4, a component of the nuclear pore complex" encoded by a nucleic

acid that hybridizes to the "NPL4, a component of the nuclear pore complex" nucleic acid or its complement under low stringency conditions,

(xxi) "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" (SEQ ID No:175) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" encoded by a nucleic acid that hybridizes to the "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" nucleic acid or its complement under low stringency conditions,

(xxii) "STRA6 isoform 1" (SEQ ID No:176) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STRA6 isoform 1" encoded by a nucleic acid that hybridizes to the "STRA6 isoform 1" nucleic acid or its complement under low stringency conditions,

(xxiii) "Tparl" (SEQ ID No:179) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Tparl" encoded by a nucleic acid that hybridizes to the "Tparl" nucleic acid or its complement under low stringency conditions, and

(xxiv) "ensp00000297280 (hypothetical protein with p-loop)" (SEQ ID No:184) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ensp00000297280 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ensp00000297280 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

14. Nucleic acid encoding a protein according to No. 13.

15. Construct, preferably a vector construct, comprising (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or

(b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative of at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the second group of proteins according to No. 1 (b).

16. Host cell, containing a vector comprising at least one of the nucleic acid of No. 14 and/or a construct of No. 15 or containing several vectors each comprising at least the nucleic acid sequence encoding at least one of the proteins, or functionally active fragments or functionally active derivatives thereof selected from the first group of proteins according to No. 1 (a) and the proteins, or functionally active fragments or functionally active derivatives thereof selected from the second group of proteins according to No. 1 (b).

17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody which binds to any of the proteins according to No. 13.

18. A kit comprising in one or more container the complex of any of No. 1 - 8 and/or the proteins of No. 13 optionally together with an antibody according to No. 17 and/or further components such as reagents and working instructions.

19. The kit according to No. 18 for processing a substrate of said complex.

20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

21. Array, in which at least a complex according to any of No. 1 - 8 and/or at least one protein according to No. 14 and/or at least one antibody according to No. 17 is attached to a solid carrier.
22. A process for processing a physiological substrate of the complex comprising the step of bringing into contact a complex to any of No. 1 - 8 with said substrate, such that said substrate is processed.
23. A pharmaceutical composition comprising the protein complex of any of No. 1 - 8 and/or any of the following the proteins:
- (i) "CDM\_HUMAN" (SEQ ID No:113) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDM\_HUMAN" encoded by a nucleic acid that hybridizes to the "CDM\_HUMAN" nucleic acid or its complement under low stringency conditions,
  - (ii) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,
  - (iii) "CGI-51" (SEQ ID No:115) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-51" encoded by a nucleic acid that hybridizes to the "CGI-51" nucleic acid or its complement under low stringency conditions,
  - (iv) "Cerebral protein 10" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cerebral protein 10" encoded by a nucleic acid that hybridizes to the "Cerebral protein 10" nucleic acid or its complement under low stringency conditions,
  - (v) "DKFZp586c1924" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DKFZp586c1924" encoded by a nucleic acid that hybridizes to the "DKFZp586c1924" nucleic acid or its complement under low stringency conditions,
  - (vi) "FLJ20342" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20342"

encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions,

(vii) "FLJ20420" (SEQ ID No:128) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20420" encoded by a nucleic acid that hybridizes to the "FLJ20420" nucleic acid or its complement under low stringency conditions,

(viii) "FLJ22555" (SEQ ID No:129) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22555" encoded by a nucleic acid that hybridizes to the "FLJ22555" nucleic acid or its complement under low stringency conditions,

(ix) "FLJ22678" (SEQ ID No:130) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22678" encoded by a nucleic acid that hybridizes to the "FLJ22678" nucleic acid or its complement under low stringency conditions,

(x) "HYPOTHETICAL PROTEIN XP\_174405" (SEQ ID No:134) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN XP\_174405" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN XP\_174405" nucleic acid or its complement under low stringency conditions,

(xi) "Hypothetical protein FLJ23356" (SEQ ID No:135) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ23356" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ23356" nucleic acid or its complement under low stringency conditions,

(xii) "Hypothetical protein KIAA0455" (SEQ ID No:136) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0455" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0455" nucleic acid or its complement under low stringency conditions,

(xiii) "Hypothetical protein KIAA0971-I" (SEQ ID No:137) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0971-I" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0971-I" nucleic acid or its complement under low stringency conditions,

- (xiv) "KIAA0062 (FRAGMENT)" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0062 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0062 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (xv) "KIAA0090" (SEQ ID No:139) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0090" encoded by a nucleic acid that hybridizes to the "KIAA0090" nucleic acid or its complement under low stringency conditions,
- (xvi) "KIAA0103" (SEQ ID No:140) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0103" encoded by a nucleic acid that hybridizes to the "KIAA0103" nucleic acid or its complement under low stringency conditions,
- (xvii) "MGC4248" (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4248" encoded by a nucleic acid that hybridizes to the "MGC4248" nucleic acid or its complement under low stringency conditions,
- (xviii) "MGC5442" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions,
- (xix) "NICE-3" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions,
- (xx) "NPL4, a component of the nuclear pore complex" (SEQ ID No:146) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPL4, a component of the nuclear pore complex" encoded by a nucleic acid that hybridizes to the "NPL4, a component of the nuclear pore complex" nucleic acid or its complement under low stringency conditions,
- (xxi) "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" (SEQ ID No:175) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" encoded by a nucleic acid that hybridizes to the "SIMILAR TO GAMMA

INTERFERON INDUCIBLE GENE IP10" nucleic acid or its complement under low stringency conditions,

(xxii) "STRA6 isoform 1" (SEQ ID No:176) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STRA6 isoform 1" encoded by a nucleic acid that hybridizes to the "STRA6 isoform 1" nucleic acid or its complement under low stringency conditions,

(xxiii) "Tparl" (SEQ ID No:179) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Tparl" encoded by a nucleic acid that hybridizes to the "Tparl" nucleic acid or its complement under low stringency conditions, and/or

(xxiv) "ensp00000297280 (hypothetical protein with p-loop)" (SEQ ID No:184) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ensp00000297280 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ensp00000297280 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions, and a pharmaceutical acceptable carrier.

24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

25. A method for screening for a molecule that binds to the complex of anyone of No. 1 - 8 and/or any of the following the proteins:

(i) "CDM\_HUMAN" (SEQ ID No:113) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDM\_HUMAN" encoded by a nucleic acid that hybridizes to the "CDM\_HUMAN" nucleic acid or its complement under low stringency conditions,

(ii) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,



- (iii) "CGI-51" (SEQ ID No:115) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-51" encoded by a nucleic acid that hybridizes to the "CGI-51" nucleic acid or its complement under low stringency conditions,
- (iv) "Cerebral protein 10" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cerebral protein 10" encoded by a nucleic acid that hybridizes to the "Cerebral protein 10" nucleic acid or its complement under low stringency conditions,
- (v) "DKFZp586c1924" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DKFZp586c1924" encoded by a nucleic acid that hybridizes to the "DKFZp586c1924" nucleic acid or its complement under low stringency conditions,
- (vi) "FLJ20342" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions,
- (vii) "FLJ20420" (SEQ ID No:128) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20420" encoded by a nucleic acid that hybridizes to the "FLJ20420" nucleic acid or its complement under low stringency conditions,
- (viii) "FLJ22555" (SEQ ID No:129) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22555" encoded by a nucleic acid that hybridizes to the "FLJ22555" nucleic acid or its complement under low stringency conditions,
- (ix) "FLJ22678" (SEQ ID No:130) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22678" encoded by a nucleic acid that hybridizes to the "FLJ22678" nucleic acid or its complement under low stringency conditions,
- (x) "HYPOTHETICAL PROTEIN XP\_174405" (SEQ ID No:134) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN XP\_174405" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN XP\_174405" nucleic acid or its complement under low stringency conditions,

- (xi) "Hypothetical protein FLJ23356" (SEQ ID No:135) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ23356" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ23356" nucleic acid or its complement under low stringency conditions,
- (xii) "Hypothetical protein KIAA0455" (SEQ ID No:136) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0455" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0455" nucleic acid or its complement under low stringency conditions,
- (xiii) "Hypothetical protein KIAA0971-I" (SEQ ID No:137) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0971-I" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0971-I" nucleic acid or its complement under low stringency conditions,
- (xiv) "KIAA0062 (FRAGMENT)" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0062 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0062 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (xv) "KIAA0090" (SEQ ID No:139) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0090" encoded by a nucleic acid that hybridizes to the "KIAA0090" nucleic acid or its complement under low stringency conditions,
- (xvi) "KIAA0103" (SEQ ID No:140) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0103" encoded by a nucleic acid that hybridizes to the "KIAA0103" nucleic acid or its complement under low stringency conditions,
- (xvii) "MGC4248" (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4248" encoded by a nucleic acid that hybridizes to the "MGC4248" nucleic acid or its complement under low stringency conditions,
- (xviii) "MGC5442" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442"

encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions,

(xix) "NICE-3" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions,

(xx) "NPL4, a component of the nuclear pore complex" (SEQ ID No:146) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPL4, a component of the nuclear pore complex" encoded by a nucleic acid that hybridizes to the "NPL4, a component of the nuclear pore complex" nucleic acid or its complement under low stringency conditions,

(xxi) "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" (SEQ ID No:175) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" encoded by a nucleic acid that hybridizes to the "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" nucleic acid or its complement under low stringency conditions,

(xxii) "STRA6 isoform 1" (SEQ ID No:176) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STRA6 isoform 1" encoded by a nucleic acid that hybridizes to the "STRA6 isoform 1" nucleic acid or its complement under low stringency conditions,

(xxiii) "Tparl" (SEQ ID No:179) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Tparl" encoded by a nucleic acid that hybridizes to the "Tparl" nucleic acid or its complement under low stringency conditions, and/or

(xxiv) "ensp00000297280 (hypothetical protein with p-loop)" (SEQ ID No:184) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ensp00000297280 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ensp00000297280 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions, comprising the steps of

(a) exposing said complex, or a cell or organism containing same to one or more candidate molecules; and

(b) determining whether said candidate molecule is bound to the complex or protein.

26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 - 8 comprising the steps of (a) exposing said complex, or a cell or organism containing Presenilin 2 complex to one or more candidate molecules; and

(b) determining the amount of activity of protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.

27. The method of No. 26, wherein the amount of said complex is determined.

28. The method of No. 26, wherein the activity of said complex is determined.

29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining the processing of said substrate is modified in the presence of said candidate molecule.

30. The method of No. 26, wherein the amount of the individual protein components of said complex are determined.

31. The method of No. 30, wherein said determining step comprises determining whether (i) "18 kDa microsomal signal peptidase subunit" (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof,

or a variant of "18 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions, and/or

(ii) "200 kDa proteasome activator" (SEQ ID No:101) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "200 kDa proteasome activator" encoded by a nucleic acid that hybridizes to the "200 kDa proteasome activator" nucleic acid or its complement under low stringency conditions, and/or

(iii) "ABCB11" (SEQ ID No:102) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ABCB11" encoded by a nucleic acid that hybridizes to the "ABCB11" nucleic acid or its complement under low stringency conditions, and/or

(iv) "ATM" (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATM" encoded by a nucleic acid that hybridizes to the "ATM" nucleic acid or its complement under low stringency conditions, and/or

(v) "ATP-binding cassette protein, sub-family B, member 1" (SEQ ID No:104) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette protein, sub-family B, member 1" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette protein, sub-family B, member 1" nucleic acid or its complement under low stringency conditions, and/or

(vi) "ATP-dependent metalloprotease FtsH1 homolog" (SEQ ID No:105) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-dependent metalloprotease FtsH1 homolog" encoded by a nucleic acid that hybridizes to the "ATP-dependent metalloprotease FtsH1 homolog" nucleic acid or its complement under low stringency conditions, and/or

(vii) "ATP7A" (SEQ ID No:106) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP7A" encoded by a nucleic acid that hybridizes to the "ATP7A" nucleic acid or its complement under low stringency conditions, and/or

(viii) "Acetolactate synthase homolog" (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Acetolactate synthase homolog" encoded by a nucleic acid that hybridizes to the

"Acetolactate synthase homolog" nucleic acid or its complement under low stringency conditions, and/or

(ix) "Adrenoleukodystrophy protein" (SEQ ID No:108) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Adrenoleukodystrophy protein" encoded by a nucleic acid that hybridizes to the "Adrenoleukodystrophy protein" nucleic acid or its complement under low stringency conditions, and/or

(x) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions, and/or

(xi) "BIG1" (SEQ ID No:110) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BIG1" encoded by a nucleic acid that hybridizes to the "BIG1" nucleic acid or its complement under low stringency conditions, and/or

(xii) "BTAF1" (SEQ ID No:111) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BTAF1" encoded by a nucleic acid that hybridizes to the "BTAF1" nucleic acid or its complement under low stringency conditions, and/or

(xiii) "CD97" (SEQ ID No:112) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CD97" encoded by a nucleic acid that hybridizes to the "CD97" nucleic acid or its complement under low stringency conditions, and/or

(xiv) "CDM\_HUMAN" (SEQ ID No:113) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDM\_HUMAN" encoded by a nucleic acid that hybridizes to the "CDM\_HUMAN" nucleic acid or its complement under low stringency conditions, and/or

(xv) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions, and/or

(xvi) "CGI-51" (SEQ ID No:115) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-51"

encoded by a nucleic acid that hybridizes to the "CGI-51" nucleic acid or its complement under low stringency conditions, and/or

(xvii) "CHRNA3" (SEQ ID No:116) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CHRNA3" encoded by a nucleic acid that hybridizes to the "CHRNA3" nucleic acid or its complement under low stringency conditions, and/or

(xviii) "Calcium-binding protein P22" (SEQ ID No:117) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calcium-binding protein P22" encoded by a nucleic acid that hybridizes to the "Calcium-binding protein P22" nucleic acid or its complement under low stringency conditions, and/or

(xix) "Cation-chloride cotransporter-interacting protein" (SEQ ID No:118) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cation-chloride cotransporter-interacting protein" encoded by a nucleic acid that hybridizes to the "Cation-chloride cotransporter-interacting protein" nucleic acid or its complement under low stringency conditions, and/or

(xx) "Centromere/kinetochore protein ZW10 homolog" (SEQ ID No:119) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Centromere/kinetochore protein ZW10 homolog" encoded by a nucleic acid that hybridizes to the "Centromere/kinetochore protein ZW10 homolog" nucleic acid or its complement under low stringency conditions, and/or

(xxi) "Cerebral protein 10" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cerebral protein 10" encoded by a nucleic acid that hybridizes to the "Cerebral protein 10" nucleic acid or its complement under low stringency conditions, and/or

(xxii) "DAAM1" (SEQ ID No:121) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DAAM1" encoded by a nucleic acid that hybridizes to the "DAAM1" nucleic acid or its complement under low stringency conditions, and/or

(xxiii) "DAPK1" (SEQ ID No:122) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DAPK1" encoded by a nucleic acid that hybridizes to the "DAPK1" nucleic acid or its complement under low stringency conditions, and/or

- (xxiv) "DKFZp586c1924" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DKFZp586c1924" encoded by a nucleic acid that hybridizes to the "DKFZp586c1924" nucleic acid or its complement under low stringency conditions, and/or
- (xxv) "DOCK3" (SEQ ID No:123) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DOCK3" encoded by a nucleic acid that hybridizes to the "DOCK3" nucleic acid or its complement under low stringency conditions, and/or
- (xxvi) "Down syndrome critical region protein 2" (SEQ ID No:124) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Down syndrome critical region protein 2" encoded by a nucleic acid that hybridizes to the "Down syndrome critical region protein 2" nucleic acid or its complement under low stringency conditions, and/or
- (xxvii) "ECSIT" (SEQ ID No:125) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ECSIT" encoded by a nucleic acid that hybridizes to the "ECSIT" nucleic acid or its complement under low stringency conditions, and/or
- (xxviii) "FACL1" (SEQ ID No:126) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FACL1" encoded by a nucleic acid that hybridizes to the "FACL1" nucleic acid or its complement under low stringency conditions, and/or
- (xxix) "FLJ20342" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions, and/or
- (xxx) "FLJ20420" (SEQ ID No:128) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20420" encoded by a nucleic acid that hybridizes to the "FLJ20420" nucleic acid or its complement under low stringency conditions, and/or
- (xxxi) "FLJ22555" (SEQ ID No:129) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22555" encoded by a nucleic acid that hybridizes to the "FLJ22555" nucleic acid or its complement under low stringency conditions, and/or



- (xxxii) "FLJ22678" (SEQ ID No:130) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22678" encoded by a nucleic acid that hybridizes to the "FLJ22678" nucleic acid or its complement under low stringency conditions, and/or
- (xxxiii) "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" (SEQ ID No:131) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" encoded by a nucleic acid that hybridizes to the "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" nucleic acid or its complement under low stringency conditions, and/or
- (xxxiv) "HTRA2" (SEQ ID No:132) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HTRA2" encoded by a nucleic acid that hybridizes to the "HTRA2" nucleic acid or its complement under low stringency conditions, and/or
- (xxxv) "HU-K4 " (SEQ ID No:133) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HU-K4 " encoded by a nucleic acid that hybridizes to the "HU-K4 " nucleic acid or its complement under low stringency conditions, and/or
- (xxxvi) "HYPOTHETICAL PROTEIN XP\_174405" (SEQ ID No:134) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN XP\_174405" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN XP\_174405" nucleic acid or its complement under low stringency conditions, and/or
- (xxxvii) "Hypothetical protein FLJ23356" (SEQ ID No:135) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ23356" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ23356" nucleic acid or its complement under low stringency conditions, and/or
- (xxxviii) "Hypothetical protein KIAA0455" (SEQ ID No:136) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0455" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0455" nucleic acid or its complement under low stringency conditions, and/or

(xxxix) "Hypothetical protein KIAA0971-I" (SEQ ID No:137) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0971-I" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0971-I" nucleic acid or its complement under low stringency conditions, and/or

(xi) "KIAA0062 (FRAGMENT)" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0062 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0062 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or

(xli) "KIAA0090" (SEQ ID No:139) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0090" encoded by a nucleic acid that hybridizes to the "KIAA0090" nucleic acid or its complement under low stringency conditions, and/or

(xlii) "KIAA0103" (SEQ ID No:140) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0103" encoded by a nucleic acid that hybridizes to the "KIAA0103" nucleic acid or its complement under low stringency conditions, and/or

(xlili) "MGC4248" (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4248" encoded by a nucleic acid that hybridizes to the "MGC4248" nucleic acid or its complement under low stringency conditions, and/or

(xliv) "MGC5442" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions, and/or

(xlv) "NICE-3" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions, and/or

(xlii) "NPC1" (SEQ ID No:144) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPC1" encoded by a nucleic acid that hybridizes to the "NPC1" nucleic acid or its complement under low stringency conditions, and/or

- (xlvii) "NPD002" (SEQ ID No:145) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPD002" encoded by a nucleic acid that hybridizes to the "NPD002" nucleic acid or its complement under low stringency conditions, and/or
- (xlviii) "NPL4, a component of the nuclear pore complex" (SEQ ID No:146) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPL4, a component of the nuclear pore complex" encoded by a nucleic acid that hybridizes to the "NPL4, a component of the nuclear pore complex" nucleic acid or its complement under low stringency conditions, and/or
- (xlix) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions, and/or
- (l) "P63 protein" (SEQ ID No:148) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "P63 protein" encoded by a nucleic acid that hybridizes to the "P63 protein" nucleic acid or its complement under low stringency conditions, and/or
- (li) "PSMA1" (SEQ ID No:149) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA1" encoded by a nucleic acid that hybridizes to the "PSMA1" nucleic acid or its complement under low stringency conditions, and/or
- (lii) "PSMA3" (SEQ ID No:150) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA3" encoded by a nucleic acid that hybridizes to the "PSMA3" nucleic acid or its complement under low stringency conditions, and/or
- (liii) "PSMA4" (SEQ ID No:151) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA4" encoded by a nucleic acid that hybridizes to the "PSMA4" nucleic acid or its complement under low stringency conditions, and/or
- (liv) "PSMA6" (SEQ ID No:152) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA6" encoded by a nucleic acid that hybridizes to the "PSMA6" nucleic acid or its complement under low stringency conditions, and/or

- (iv) "PSMB1" (SEQ ID No:153) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB1" encoded by a nucleic acid that hybridizes to the "PSMB1" nucleic acid or its complement under low stringency conditions, and/or
- (lvi) "PSMB2" (SEQ ID No:154) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB2" encoded by a nucleic acid that hybridizes to the "PSMB2" nucleic acid or its complement under low stringency conditions, and/or
- (lvii) "PSMB3" (SEQ ID No:155) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB3" encoded by a nucleic acid that hybridizes to the "PSMB3" nucleic acid or its complement under low stringency conditions, and/or
- (lviii) "PSMB4" (SEQ ID No:156) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB4" encoded by a nucleic acid that hybridizes to the "PSMB4" nucleic acid or its complement under low stringency conditions, and/or
- (lix) "PSMB5" (SEQ ID No:157) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB5" encoded by a nucleic acid that hybridizes to the "PSMB5" nucleic acid or its complement under low stringency conditions, and/or
- (lx) "PSMB6" (SEQ ID No:158) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB6" encoded by a nucleic acid that hybridizes to the "PSMB6" nucleic acid or its complement under low stringency conditions, and/or
- (lxi) "PSMC1" (SEQ ID No:159) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC1" encoded by a nucleic acid that hybridizes to the "PSMC1" nucleic acid or its complement under low stringency conditions, and/or
- (lxii) "PSMC2" (SEQ ID No:160) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC2" encoded by a nucleic acid that hybridizes to the "PSMC2" nucleic acid or its complement under low stringency conditions, and/or
- (lxiii) "PSMC3" (SEQ ID No:161) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC3"

encoded by a nucleic acid that hybridizes to the "PSMC3" nucleic acid or its complement under low stringency conditions, and/or

(lxiv) "PSMC4" (SEQ ID No:162) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC4" encoded by a nucleic acid that hybridizes to the "PSMC4" nucleic acid or its complement under low stringency conditions, and/or

(lxv) "PSMC5" (SEQ ID No:163) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC5" encoded by a nucleic acid that hybridizes to the "PSMC5" nucleic acid or its complement under low stringency conditions, and/or

(lxvi) "PSMC6" (SEQ ID No:164) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC6" encoded by a nucleic acid that hybridizes to the "PSMC6" nucleic acid or its complement under low stringency conditions, and/or

(lxvii) "PSMD1" (SEQ ID No:165) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD1" encoded by a nucleic acid that hybridizes to the "PSMD1" nucleic acid or its complement under low stringency conditions, and/or

(lxviii) "PSMD11" (SEQ ID No:166) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD11" encoded by a nucleic acid that hybridizes to the "PSMD11" nucleic acid or its complement under low stringency conditions, and/or

(lxix) "PSMD12" (SEQ ID No:167) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD12" encoded by a nucleic acid that hybridizes to the "PSMD12" nucleic acid or its complement under low stringency conditions, and/or

(lxx) "PSMD13" (SEQ ID No:168) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD13" encoded by a nucleic acid that hybridizes to the "PSMD13" nucleic acid or its complement under low stringency conditions, and/or

(lxxi) "PSMD2" (SEQ ID No:169) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD2" encoded by a nucleic acid that hybridizes to the "PSMD2" nucleic acid or its complement under low stringency conditions, and/or

(lxxii) "PSMD3" (SEQ ID No:170) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD3" encoded by a nucleic acid that hybridizes to the "PSMD3" nucleic acid or its complement under low stringency conditions, and/or

(lxxiii) "PSMD4" (SEQ ID No:171) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD4" encoded by a nucleic acid that hybridizes to the "PSMD4" nucleic acid or its complement under low stringency conditions, and/or

(lxxiv) "Presenilin 2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions, and/or

(lxxv) "Prohibitin" (SEQ ID No:173) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Prohibitin" encoded by a nucleic acid that hybridizes to the "Prohibitin" nucleic acid or its complement under low stringency conditions, and/or

(lxxvi) "RPS6KA3" (SEQ ID No:174) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RPS6KA3" encoded by a nucleic acid that hybridizes to the "RPS6KA3" nucleic acid or its complement under low stringency conditions, and/or

(lxxvii) "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" (SEQ ID No:175) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" encoded by a nucleic acid that hybridizes to the "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" nucleic acid or its complement under low stringency conditions, and/or

(lxxviii) "STRA6 isoform 1" (SEQ ID No:176) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STRA6 isoform 1" encoded by a nucleic acid that hybridizes to the "STRA6 isoform 1" nucleic acid or its complement under low stringency conditions, and/or

(lxxix) "Serine/threonine protein phosphatase 6" (SEQ ID No:90) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Serine/threonine protein phosphatase 6" encoded by a nucleic acid that

hybridizes to the "Serine/threonine protein phosphatase 6" nucleic acid or its complement under low stringency conditions, and/or

(lxxx) "Sortilin 1" (SEQ ID No:177) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sortilin 1" encoded by a nucleic acid that hybridizes to the "Sortilin 1" nucleic acid or its complement under low stringency conditions, and/or

(lxxxi) "Stearoyl-CoA desaturase" (SEQ ID No:178) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Stearoyl-CoA desaturase" encoded by a nucleic acid that hybridizes to the "Stearoyl-CoA desaturase" nucleic acid or its complement under low stringency conditions, and/or

(lxxxii) "Tparl" (SEQ ID No:179) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Tparl" encoded by a nucleic acid that hybridizes to the "Tparl" nucleic acid or its complement under low stringency conditions, and/or

(lxxxiii) "Ubiquitin-protein ligase EDD" (SEQ ID No:180) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Ubiquitin-protein ligase EDD" encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase EDD" nucleic acid or its complement under low stringency conditions, and/or

(lxxxiv) "Voltage-dependent anion channel 2" (SEQ ID No:181) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Voltage-dependent anion channel 2" encoded by a nucleic acid that hybridizes to the "Voltage-dependent anion channel 2" nucleic acid or its complement under low stringency conditions, and/or

(lxxxv) "Wolframin" (SEQ ID No:182) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Wolframin" encoded by a nucleic acid that hybridizes to the "Wolframin" nucleic acid or its complement under low stringency conditions, and/or

(lxxxvi) "cholinergic receptor, nicotinic, alpha polypeptide 3" (SEQ ID No:183) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "cholinergic receptor, nicotinic, alpha polypeptide 3" encoded by a nucleic acid that hybridizes to the "cholinergic receptor, nicotinic, alpha polypeptide 3" nucleic acid or its complement under low stringency conditions, and/or

(lxxxvii) "ensp00000297280 (hypothetical protein with p-loop)" (SEQ ID No:184) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ensp00000297280 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ensp00000297280 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions, is present in the complex.

32. The method of any of No. 26 - 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 - 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

34. A method for the production of a pharmaceutical composition comprising carrying out the method of any of No. 1 - 8 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.

35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, activity of, or component composition of, or intracellular localization of the complex of any one of the No. 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in an analogous sample from a subject not having the disease or disorder or predisposition indicates the presence in the subject of the disease or disorder or predisposition in the subject.



36. The method of No. 35, wherein the amount of said complex is determined.

37. The method of No. 35, wherein the activity of said complex is determined.

38. The method of No. 37, wherein said determining step comprises isolating from the subject said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.

39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.

40. The method of No. 39, wherein said determining step comprises determining whether (i) "18 kDa microsomal signal peptidase subunit" (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "18 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions, and/or

(ii) "200 kDa proteasome activator" (SEQ ID No:101) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "200 kDa proteasome activator" encoded by a nucleic acid that hybridizes to the "200 kDa proteasome activator" nucleic acid or its complement under low stringency conditions, and/or

(iii) "ABCB11" (SEQ ID No:102) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ABCB11" encoded by a nucleic acid that hybridizes to the "ABCB11" nucleic acid or its complement under low stringency conditions, and/or

(iv) "ATM" (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATM" encoded by a nucleic acid that hybridizes to the "ATM" nucleic acid or its complement under low stringency conditions, and/or

- (v) "ATP-binding cassette protein, sub-family B, member 1" (SEQ ID No:104) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette protein, sub-family B, member 1" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette protein, sub-family B, member 1" nucleic acid or its complement under low stringency conditions, and/or
- (vi) "ATP-dependent metalloprotease FtsH1 homolog" (SEQ ID No:105) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-dependent metalloprotease FtsH1 homolog" encoded by a nucleic acid that hybridizes to the "ATP-dependent metalloprotease FtsH1 homolog" nucleic acid or its complement under low stringency conditions, and/or
- (vii) "ATP7A" (SEQ ID No:106) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP7A" encoded by a nucleic acid that hybridizes to the "ATP7A" nucleic acid or its complement under low stringency conditions, and/or
- (viii) "Acetolactate synthase homolog" (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Acetolactate synthase homolog" encoded by a nucleic acid that hybridizes to the "Acetolactate synthase homolog" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "Adrenoleukodystrophy protein" (SEQ ID No:108) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Adrenoleukodystrophy protein" encoded by a nucleic acid that hybridizes to the "Adrenoleukodystrophy protein" nucleic acid or its complement under low stringency conditions, and/or
- (x) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "BIG1" (SEQ ID No:110) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BIG1" encoded by a nucleic acid that hybridizes to the "BIG1" nucleic acid or its complement under low stringency conditions, and/or

- (xii) "BTAF1" (SEQ ID No:111) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BTAF1" encoded by a nucleic acid that hybridizes to the "BTAF1" nucleic acid or its complement under low stringency conditions, and/or
- (xiii) "CD97" (SEQ ID No:112) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CD97" encoded by a nucleic acid that hybridizes to the "CD97" nucleic acid or its complement under low stringency conditions, and/or
- (xiv) "CDM\_HUMAN" (SEQ ID No:113) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDM\_HUMAN" encoded by a nucleic acid that hybridizes to the "CDM\_HUMAN" nucleic acid or its complement under low stringency conditions, and/or
- (xv) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions, and/or
- (xvi) "CGI-51" (SEQ ID No:115) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-51" encoded by a nucleic acid that hybridizes to the "CGI-51" nucleic acid or its complement under low stringency conditions, and/or
- (xvii) "CHRNA3" (SEQ ID No:116) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CHRNA3" encoded by a nucleic acid that hybridizes to the "CHRNA3" nucleic acid or its complement under low stringency conditions, and/or
- (xviii) "Calcium-binding protein P22" (SEQ ID No:117) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calcium-binding protein P22" encoded by a nucleic acid that hybridizes to the "Calcium-binding protein P22" nucleic acid or its complement under low stringency conditions, and/or
- (xix) "Cation-chloride cotransporter-interacting protein" (SEQ ID No:118) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cation-chloride cotransporter-interacting protein" encoded by a nucleic acid that hybridizes to the "Cation-chloride cotransporter-interacting protein" nucleic acid or its complement under low stringency conditions, and/or

(xx) "Centromere/kinetochore protein ZW10 homolog" (SEQ ID No:119) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Centromere/kinetochore protein ZW10 homolog" encoded by a nucleic acid that hybridizes to the "Centromere/kinetochore protein ZW10 homolog" nucleic acid or its complement under low stringency conditions, and/or

(xxi) "Cerebral protein 10" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cerebral protein 10" encoded by a nucleic acid that hybridizes to the "Cerebral protein 10" nucleic acid or its complement under low stringency conditions, and/or

(xxii) "DAAM1" (SEQ ID No:121) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DAAM1" encoded by a nucleic acid that hybridizes to the "DAAM1" nucleic acid or its complement under low stringency conditions, and/or

(xxiii) "DAPK1" (SEQ ID No:122) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DAPK1" encoded by a nucleic acid that hybridizes to the "DAPK1" nucleic acid or its complement under low stringency conditions, and/or

(xxiv) "DKFZp586c1924" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DKFZp586c1924" encoded by a nucleic acid that hybridizes to the "DKFZp586c1924" nucleic acid or its complement under low stringency conditions, and/or

(xxv) "DOCK3" (SEQ ID No:123) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DOCK3" encoded by a nucleic acid that hybridizes to the "DOCK3" nucleic acid or its complement under low stringency conditions, and/or

(xxvi) "Down syndrome critical region protein 2" (SEQ ID No:124) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Down syndrome critical region protein 2" encoded by a nucleic acid that hybridizes to the "Down syndrome critical region protein 2" nucleic acid or its complement under low stringency conditions, and/or

(xxvii) "ECSIT" (SEQ ID No:125) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ECSIT" encoded by a nucleic acid that hybridizes to the "ECSIT" nucleic acid or its complement under low stringency conditions, and/or

(xxviii) "FACL1" (SEQ ID No:126) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FACL1" encoded by a nucleic acid that hybridizes to the "FACL1" nucleic acid or its complement under low stringency conditions, and/or

(xxix) "FLJ20342" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions, and/or

(xxx) "FLJ20420" (SEQ ID No:128) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20420" encoded by a nucleic acid that hybridizes to the "FLJ20420" nucleic acid or its complement under low stringency conditions, and/or

(xxxi) "FLJ22555" (SEQ ID No:129) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22555" encoded by a nucleic acid that hybridizes to the "FLJ22555" nucleic acid or its complement under low stringency conditions, and/or

(xxxii) "FLJ22678" (SEQ ID No:130) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22678" encoded by a nucleic acid that hybridizes to the "FLJ22678" nucleic acid or its complement under low stringency conditions, and/or

(xxxiii) "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" (SEQ ID No:131) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" encoded by a nucleic acid that hybridizes to the "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" nucleic acid or its complement under low stringency conditions, and/or

(xxxiv) "HTRA2" (SEQ ID No:132) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HTRA2" encoded by a nucleic acid that hybridizes to the "HTRA2" nucleic acid or its complement under low stringency conditions, and/or

(xxxv) "HU-K4 " (SEQ ID No:133) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HU-K4 " encoded by a nucleic acid that hybridizes to the "HU-K4 " nucleic acid or its complement under low stringency conditions, and/or

(xxxvi) "HYPOTHETICAL PROTEIN XP\_174405" (SEQ ID No:134) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN XP\_174405" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN XP\_174405" nucleic acid or its complement under low stringency conditions, and/or

(xxxvii) "Hypothetical protein FLJ23356" (SEQ ID No:135) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ23356" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ23356" nucleic acid or its complement under low stringency conditions, and/or

(xxxviii) "Hypothetical protein KIAA0455" (SEQ ID No:136) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0455" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0455" nucleic acid or its complement under low stringency conditions, and/or

(xxxix) "Hypothetical protein KIAA0971-I" (SEQ ID No:137) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0971-I" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0971-I" nucleic acid or its complement under low stringency conditions, and/or

(xl) "KIAA0062 (FRAGMENT)" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0062 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0062 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or

(xli) "KIAA0090" (SEQ ID No:139) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0090" encoded by a nucleic acid that hybridizes to the "KIAA0090" nucleic acid or its complement under low stringency conditions, and/or

(xlii) "KIAA0103" (SEQ ID No:140) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0103" encoded by a nucleic acid that hybridizes to the "KIAA0103" nucleic acid or its complement under low stringency conditions, and/or

(xliii) "MGC4248" (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4248"

encoded by a nucleic acid that hybridizes to the "MGC4248" nucleic acid or its complement under low stringency conditions, and/or

(xlv) "MGC5442" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions, and/or

(xlv) "NICE-3" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions, and/or

(xlv) "NPC1" (SEQ ID No:144) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPC1" encoded by a nucleic acid that hybridizes to the "NPC1" nucleic acid or its complement under low stringency conditions, and/or

(xlvii) "NPD002" (SEQ ID No:145) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPD002" encoded by a nucleic acid that hybridizes to the "NPD002" nucleic acid or its complement under low stringency conditions, and/or

(xlviii) "NPL4, a component of the nuclear pore complex" (SEQ ID No:146) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPL4, a component of the nuclear pore complex" encoded by a nucleic acid that hybridizes to the "NPL4, a component of the nuclear pore complex" nucleic acid or its complement under low stringency conditions, and/or

(xlix) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions, and/or

(l) "P63 protein" (SEQ ID No:148) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "P63 protein" encoded by a nucleic acid that hybridizes to the "P63 protein" nucleic acid or its complement under low stringency conditions, and/or

(ii) "PSMA1" (SEQ ID No:149) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA1" encoded by a

nucleic acid that hybridizes to the "PSMA1" nucleic acid or its complement under low stringency conditions, and/or

(lii) "PSMA3" (SEQ ID No:150) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA3" encoded by a nucleic acid that hybridizes to the "PSMA3" nucleic acid or its complement under low stringency conditions, and/or

(liii) "PSMA4" (SEQ ID No:151) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA4" encoded by a nucleic acid that hybridizes to the "PSMA4" nucleic acid or its complement under low stringency conditions, and/or

(liv) "PSMA6" (SEQ ID No:152) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA6" encoded by a nucleic acid that hybridizes to the "PSMA6" nucleic acid or its complement under low stringency conditions, and/or

(lv) "PSMB1" (SEQ ID No:153) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB1" encoded by a nucleic acid that hybridizes to the "PSMB1" nucleic acid or its complement under low stringency conditions, and/or

(lvi) "PSMB2" (SEQ ID No:154) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB2" encoded by a nucleic acid that hybridizes to the "PSMB2" nucleic acid or its complement under low stringency conditions, and/or

(lvii) "PSMB3" (SEQ ID No:155) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB3" encoded by a nucleic acid that hybridizes to the "PSMB3" nucleic acid or its complement under low stringency conditions, and/or

(lviii) "PSMB4" (SEQ ID No:156) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB4" encoded by a nucleic acid that hybridizes to the "PSMB4" nucleic acid or its complement under low stringency conditions, and/or

(lix) "PSMB5" (SEQ ID No:157) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB5" encoded by a nucleic acid that hybridizes to the "PSMB5" nucleic acid or its complement under low stringency conditions, and/or



(lx) "PSMB6" (SEQ ID No:158) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB6" encoded by a nucleic acid that hybridizes to the "PSMB6" nucleic acid or its complement under low stringency conditions, and/or

(lxi) "PSMC1" (SEQ ID No:159) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC1" encoded by a nucleic acid that hybridizes to the "PSMC1" nucleic acid or its complement under low stringency conditions, and/or

(lxii) "PSMC2" (SEQ ID No:160) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC2" encoded by a nucleic acid that hybridizes to the "PSMC2" nucleic acid or its complement under low stringency conditions, and/or

(lxiii) "PSMC3" (SEQ ID No:161) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC3" encoded by a nucleic acid that hybridizes to the "PSMC3" nucleic acid or its complement under low stringency conditions, and/or

(lxiv) "PSMC4" (SEQ ID No:162) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC4" encoded by a nucleic acid that hybridizes to the "PSMC4" nucleic acid or its complement under low stringency conditions, and/or

(lxv) "PSMC5" (SEQ ID No:163) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC5" encoded by a nucleic acid that hybridizes to the "PSMC5" nucleic acid or its complement under low stringency conditions, and/or

(lxvi) "PSMC6" (SEQ ID No:164) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC6" encoded by a nucleic acid that hybridizes to the "PSMC6" nucleic acid or its complement under low stringency conditions, and/or

(lxvii) "PSMD1" (SEQ ID No:165) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD1" encoded by a nucleic acid that hybridizes to the "PSMD1" nucleic acid or its complement under low stringency conditions, and/or

(lxviii) "PSMD11" (SEQ ID No:166) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD11"

encoded by a nucleic acid that hybridizes to the "PSMD11" nucleic acid or its complement under low stringency conditions, and/or

(lix) "PSMD12" (SEQ ID No:167) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD12" encoded by a nucleic acid that hybridizes to the "PSMD12" nucleic acid or its complement under low stringency conditions, and/or

(lxx) "PSMD13" (SEQ ID No:168) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD13" encoded by a nucleic acid that hybridizes to the "PSMD13" nucleic acid or its complement under low stringency conditions, and/or

(lxxi) "PSMD2" (SEQ ID No:169) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD2" encoded by a nucleic acid that hybridizes to the "PSMD2" nucleic acid or its complement under low stringency conditions, and/or

(lxxii) "PSMD3" (SEQ ID No:170) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD3" encoded by a nucleic acid that hybridizes to the "PSMD3" nucleic acid or its complement under low stringency conditions, and/or

(lxxiii) "PSMD4" (SEQ ID No:171) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD4" encoded by a nucleic acid that hybridizes to the "PSMD4" nucleic acid or its complement under low stringency conditions, and/or

(lxxiv) "Presenilin 2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions, and/or

(lxxv) "Prohibitin" (SEQ ID No:173) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Prohibitin" encoded by a nucleic acid that hybridizes to the "Prohibitin" nucleic acid or its complement under low stringency conditions, and/or

(lxxvi) "RPS6KA3" (SEQ ID No:174) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RPS6KA3" encoded by a nucleic acid that hybridizes to the "RPS6KA3" nucleic acid or its complement under low stringency conditions, and/or

(lxxvii) "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" (SEQ ID No:175) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" encoded by a nucleic acid that hybridizes to the "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" nucleic acid or its complement under low stringency conditions, and/or

(lxxviii) "STRA6 isoform 1" (SEQ ID No:176) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STRA6 isoform 1" encoded by a nucleic acid that hybridizes to the "STRA6 isoform 1" nucleic acid or its complement under low stringency conditions, and/or

(lxxix) "Serine/threonine protein phosphatase 6" (SEQ ID No:90) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Serine/threonine protein phosphatase 6" encoded by a nucleic acid that hybridizes to the "Serine/threonine protein phosphatase 6" nucleic acid or its complement under low stringency conditions, and/or

(lxxx) "Sortilin 1" (SEQ ID No:177) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sortilin 1" encoded by a nucleic acid that hybridizes to the "Sortilin 1" nucleic acid or its complement under low stringency conditions, and/or

(lxxxi) "Stearoyl-CoA desaturase" (SEQ ID No:178) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Stearoyl-CoA desaturase" encoded by a nucleic acid that hybridizes to the "Stearoyl-CoA desaturase" nucleic acid or its complement under low stringency conditions, and/or

(lxxxii) "Tparl" (SEQ ID No:179) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Tparl" encoded by a nucleic acid that hybridizes to the "Tparl" nucleic acid or its complement under low stringency conditions, and/or

(lxxxiii) "Ubiquitin-protein ligase EDD" (SEQ ID No:180) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Ubiquitin-protein ligase EDD" encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase EDD" nucleic acid or its complement under low stringency conditions, and/or

(lxxxiv) "Voltage-dependent anion channel 2" (SEQ ID No:181) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a

variant of "Voltage-dependent anion channel 2" encoded by a nucleic acid that hybridizes to the "Voltage-dependent anion channel 2" nucleic acid or its complement under low stringency conditions, and/or

(lxxxv) "Wolframin" (SEQ ID No:182) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Wolframin" encoded by a nucleic acid that hybridizes to the "Wolframin" nucleic acid or its complement under low stringency conditions, and/or

(lxxxvi) "cholinergic receptor, nicotinic, alpha polypeptide 3" (SEQ ID No:183) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "cholinergic receptor, nicotinic, alpha polypeptide 3" encoded by a nucleic acid that hybridizes to the "cholinergic receptor, nicotinic, alpha polypeptide 3" nucleic acid or its complement under low stringency conditions, and/or

(lxxxvii) "ensp00000297280 (hypothetical protein with p-loop)" (SEQ ID No:184) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ensp00000297280 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ensp00000297280 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions, is present in the complex.

41. The complex of any one of No. 1 - 8, or proteins of No. 13 or the antibody or fragment of No. 17, for use in a method of diagnosing a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity or component composition of or intracellular localization of, the complex of anyone of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi

(siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), or protein components of, said complex.

43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.

44. The method according to No. 42, wherein said disease or disorder involves increased levels of the amount or activity of said complex.

45. Complex of any of No. 1 - 8 and/or protein selected from the following proteins

(i) "18 kDa microsomal signal peptidase subunit" (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "18 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,

(ii) "200 kDa proteasome activator" (SEQ ID No:101) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "200 kDa proteasome activator" encoded by a nucleic acid that hybridizes to the "200 kDa proteasome activator" nucleic acid or its complement under low stringency conditions,

(iii) "ABCB11" (SEQ ID No:102) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ABCB11" encoded by a nucleic acid that hybridizes to the "ABCB11" nucleic acid or its complement under low stringency conditions,

(iv) "ATM" (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATM" encoded by a nucleic acid that hybridizes to the "ATM" nucleic acid or its complement under low stringency conditions,

- (v) "ATP-binding cassette protein, sub-family B, member 1" (SEQ ID No:104) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette protein, sub-family B, member 1" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette protein, sub-family B, member 1" nucleic acid or its complement under low stringency conditions,
- (vi) "ATP-dependent metalloprotease FtsH1 homolog" (SEQ ID No:105) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-dependent metalloprotease FtsH1 homolog" encoded by a nucleic acid that hybridizes to the "ATP-dependent metalloprotease FtsH1 homolog" nucleic acid or its complement under low stringency conditions,
- (vii) "ATP7A" (SEQ ID No:106) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP7A" encoded by a nucleic acid that hybridizes to the "ATP7A" nucleic acid or its complement under low stringency conditions,
- (viii) "Acetolactate synthase homolog" (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Acetolactate synthase homolog" encoded by a nucleic acid that hybridizes to the "Acetolactate synthase homolog" nucleic acid or its complement under low stringency conditions,
- (ix) "Adrenoleukodystrophy protein" (SEQ ID No:108) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Adrenoleukodystrophy protein" encoded by a nucleic acid that hybridizes to the "Adrenoleukodystrophy protein" nucleic acid or its complement under low stringency conditions,
- (x) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,
- (xi) "BIG1" (SEQ ID No:110) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BIG1" encoded by a nucleic acid that hybridizes to the "BIG1" nucleic acid or its complement under low stringency conditions,
- (xii) "BTAF1" (SEQ ID No:111) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BTAF1" encoded by a

nucleic acid that hybridizes to the "BTAF1" nucleic acid or its complement under low stringency conditions,

(xiii) "CD97" (SEQ ID No:112) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CD97" encoded by a nucleic acid that hybridizes to the "CD97" nucleic acid or its complement under low stringency conditions,

(xiv) "CDM\_HUMAN" (SEQ ID No:113) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDM\_HUMAN" encoded by a nucleic acid that hybridizes to the "CDM\_HUMAN" nucleic acid or its complement under low stringency conditions,

(xv) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,

(xvi) "CGI-51" (SEQ ID No:115) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-51" encoded by a nucleic acid that hybridizes to the "CGI-51" nucleic acid or its complement under low stringency conditions,

(xvii) "CHRNA3" (SEQ ID No:116) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CHRNA3" encoded by a nucleic acid that hybridizes to the "CHRNA3" nucleic acid or its complement under low stringency conditions,

(xviii) "Calcium-binding protein P22" (SEQ ID No:117) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calcium-binding protein P22" encoded by a nucleic acid that hybridizes to the "Calcium-binding protein P22" nucleic acid or its complement under low stringency conditions,

(xix) "Cation-chloride cotransporter-interacting protein" (SEQ ID No:118) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cation-chloride cotransporter-interacting protein" encoded by a nucleic acid that hybridizes to the "Cation-chloride cotransporter-interacting protein" nucleic acid or its complement under low stringency conditions,

(xx) "Centromere/kinetochore protein ZW10 homolog" (SEQ ID No:119) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Centromere/kinetochore protein ZW10 homolog" encoded by a nucleic

acid that hybridizes to the "Centromere/kinetochore protein ZW10 homolog" nucleic acid or its complement under low stringency conditions,

(xxi) "Cerebral protein 10" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cerebral protein 10" encoded by a nucleic acid that hybridizes to the "Cerebral protein 10" nucleic acid or its complement under low stringency conditions,

(xxii) "DAAM1" (SEQ ID No:121) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DAAM1" encoded by a nucleic acid that hybridizes to the "DAAM1" nucleic acid or its complement under low stringency conditions,

(xxiii) "DAPK1" (SEQ ID No:122) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DAPK1" encoded by a nucleic acid that hybridizes to the "DAPK1" nucleic acid or its complement under low stringency conditions,

(xxiv) "DKFZp586c1924" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DKFZp586c1924" encoded by a nucleic acid that hybridizes to the "DKFZp586c1924" nucleic acid or its complement under low stringency conditions,

(xxv) "DOCK3" (SEQ ID No:123) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DOCK3" encoded by a nucleic acid that hybridizes to the "DOCK3" nucleic acid or its complement under low stringency conditions,

(xxvi) "Down syndrome critical region protein 2" (SEQ ID No:124) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Down syndrome critical region protein 2" encoded by a nucleic acid that hybridizes to the "Down syndrome critical region protein 2" nucleic acid or its complement under low stringency conditions,

(xxvii) "ECSIT" (SEQ ID No:125) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ECSIT" encoded by a nucleic acid that hybridizes to the "ECSIT" nucleic acid or its complement under low stringency conditions,

(xxviii) "FACL1" (SEQ ID No:126) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FACL1"



encoded by a nucleic acid that hybridizes to the "FACL1" nucleic acid or its complement under low stringency conditions,

(xxix) "FLJ20342" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions,

(xxx) "FLJ20420" (SEQ ID No:128) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20420" encoded by a nucleic acid that hybridizes to the "FLJ20420" nucleic acid or its complement under low stringency conditions,

(xxxi) "FLJ22555" (SEQ ID No:129) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22555" encoded by a nucleic acid that hybridizes to the "FLJ22555" nucleic acid or its complement under low stringency conditions,

(xxxii) "FLJ22678" (SEQ ID No:130) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22678" encoded by a nucleic acid that hybridizes to the "FLJ22678" nucleic acid or its complement under low stringency conditions,

(xxxiii) "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" (SEQ ID No:131) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" encoded by a nucleic acid that hybridizes to the "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" nucleic acid or its complement under low stringency conditions,

(xxxiv) "HTRA2" (SEQ ID No:132) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HTRA2" encoded by a nucleic acid that hybridizes to the "HTRA2" nucleic acid or its complement under low stringency conditions,

(xxxv) "HU-K4 " (SEQ ID No:133) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HU-K4 " encoded by a nucleic acid that hybridizes to the "HU-K4 " nucleic acid or its complement under low stringency conditions,

(xxxvi) "HYPOTHETICAL PROTEIN XP\_174405" (SEQ ID No:134) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof,

or a variant of "HYPOTHETICAL PROTEIN XP\_174405" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN XP\_174405" nucleic acid or its complement under low stringency conditions,

(xxxvii) "Hypothetical protein FLJ23356" (SEQ ID No:135) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ23356" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ23356" nucleic acid or its complement under low stringency conditions,

(xxxviii) "Hypothetical protein KIAA0455" (SEQ ID No:136) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0455" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0455" nucleic acid or its complement under low stringency conditions,

(xxxix) "Hypothetical protein KIAA0971-I" (SEQ ID No:137) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0971-I" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0971-I" nucleic acid or its complement under low stringency conditions,

(xl) "KIAA0062 (FRAGMENT)" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0062 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0062 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xli) "KIAA0090" (SEQ ID No:139) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0090" encoded by a nucleic acid that hybridizes to the "KIAA0090" nucleic acid or its complement under low stringency conditions,

(xlii) "KIAA0103" (SEQ ID No:140) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0103" encoded by a nucleic acid that hybridizes to the "KIAA0103" nucleic acid or its complement under low stringency conditions,

(xlili) "MGC4248" (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4248" encoded by a nucleic acid that hybridizes to the "MGC4248" nucleic acid or its complement under low stringency conditions,

- (xliv) "MGC5442" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions,
- (xlv) "NICE-3" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions,
- (xlvi) "NPC1" (SEQ ID No:144) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPC1" encoded by a nucleic acid that hybridizes to the "NPC1" nucleic acid or its complement under low stringency conditions,
- (xlvii) "NPD002" (SEQ ID No:145) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPD002" encoded by a nucleic acid that hybridizes to the "NPD002" nucleic acid or its complement under low stringency conditions,
- (xlviii) "NPL4, a component of the nuclear pore complex" (SEQ ID No:146) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPL4, a component of the nuclear pore complex" encoded by a nucleic acid that hybridizes to the "NPL4, a component of the nuclear pore complex" nucleic acid or its complement under low stringency conditions,
- (xlix) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,
- (l) "P63 protein" (SEQ ID No:148) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "P63 protein" encoded by a nucleic acid that hybridizes to the "P63 protein" nucleic acid or its complement under low stringency conditions,
- (li) "PSMA1" (SEQ ID No:149) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA1" encoded by a nucleic acid that hybridizes to the "PSMA1" nucleic acid or its complement under low stringency conditions,

(iii) "PSMA3" (SEQ ID No:150) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA3" encoded by a nucleic acid that hybridizes to the "PSMA3" nucleic acid or its complement under low stringency conditions,

(liii) "PSMA4" (SEQ ID No:151) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA4" encoded by a nucleic acid that hybridizes to the "PSMA4" nucleic acid or its complement under low stringency conditions,

(liv) "PSMA6" (SEQ ID No:152) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA6" encoded by a nucleic acid that hybridizes to the "PSMA6" nucleic acid or its complement under low stringency conditions,

(lv) "PSMB1" (SEQ ID No:153) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB1" encoded by a nucleic acid that hybridizes to the "PSMB1" nucleic acid or its complement under low stringency conditions,

(lvi) "PSMB2" (SEQ ID No:154) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB2" encoded by a nucleic acid that hybridizes to the "PSMB2" nucleic acid or its complement under low stringency conditions,

(lvii) "PSMB3" (SEQ ID No:155) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB3" encoded by a nucleic acid that hybridizes to the "PSMB3" nucleic acid or its complement under low stringency conditions,

(lviii) "PSMB4" (SEQ ID No:156) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB4" encoded by a nucleic acid that hybridizes to the "PSMB4" nucleic acid or its complement under low stringency conditions,

(lix) "PSMB5" (SEQ ID No:157) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB5" encoded by a nucleic acid that hybridizes to the "PSMB5" nucleic acid or its complement under low stringency conditions,

(lx) "PSMB6" (SEQ ID No:158) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB6" encoded by a

nucleic acid that hybridizes to the "PSMB6" nucleic acid or its complement under low stringency conditions,

(lxi) "PSMC1" (SEQ ID No:159) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC1" encoded by a nucleic acid that hybridizes to the "PSMC1" nucleic acid or its complement under low stringency conditions,

(lxii) "PSMC2" (SEQ ID No:160) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC2" encoded by a nucleic acid that hybridizes to the "PSMC2" nucleic acid or its complement under low stringency conditions,

(lxiii) "PSMC3" (SEQ ID No:161) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC3" encoded by a nucleic acid that hybridizes to the "PSMC3" nucleic acid or its complement under low stringency conditions,

(lxiv) "PSMC4" (SEQ ID No:162) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC4" encoded by a nucleic acid that hybridizes to the "PSMC4" nucleic acid or its complement under low stringency conditions,

(lxv) "PSMC5" (SEQ ID No:163) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC5" encoded by a nucleic acid that hybridizes to the "PSMC5" nucleic acid or its complement under low stringency conditions,

(lxvi) "PSMC6" (SEQ ID No:164) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC6" encoded by a nucleic acid that hybridizes to the "PSMC6" nucleic acid or its complement under low stringency conditions,

(lxvii) "PSMD1" (SEQ ID No:165) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD1" encoded by a nucleic acid that hybridizes to the "PSMD1" nucleic acid or its complement under low stringency conditions,

(lxviii) "PSMD11" (SEQ ID No:166) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD11" encoded by a nucleic acid that hybridizes to the "PSMD11" nucleic acid or its complement under low stringency conditions,

(Ixxix) "PSMD12" (SEQ ID No:167) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD12" encoded by a nucleic acid that hybridizes to the "PSMD12" nucleic acid or its complement under low stringency conditions,

(Ixx) "PSMD13" (SEQ ID No:168) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD13" encoded by a nucleic acid that hybridizes to the "PSMD13" nucleic acid or its complement under low stringency conditions,

(Ixxi) "PSMD2" (SEQ ID No:169) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD2" encoded by a nucleic acid that hybridizes to the "PSMD2" nucleic acid or its complement under low stringency conditions,

(Ixxii) "PSMD3" (SEQ ID No:170) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD3" encoded by a nucleic acid that hybridizes to the "PSMD3" nucleic acid or its complement under low stringency conditions,

(Ixxiii) "PSMD4" (SEQ ID No:171) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD4" encoded by a nucleic acid that hybridizes to the "PSMD4" nucleic acid or its complement under low stringency conditions,

(Ixxiv) "Presenilin 2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions,

(Ixxv) "Prohibitin" (SEQ ID No:173) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Prohibitin" encoded by a nucleic acid that hybridizes to the "Prohibitin" nucleic acid or its complement under low stringency conditions,

(Ixxvi) "RPS6KA3" (SEQ ID No:174) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RPS6KA3" encoded by a nucleic acid that hybridizes to the "RPS6KA3" nucleic acid or its complement under low stringency conditions,

(Ixxvii) "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" (SEQ ID No:175) or a functionally active derivative thereof, or a functionally active fragment thereof, or a

homolog thereof, or a variant of "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" encoded by a nucleic acid that hybridizes to the "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" nucleic acid or its complement under low stringency conditions,

(lxxviii) "STRA6 isoform 1" (SEQ ID No:176) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STRA6 isoform 1" encoded by a nucleic acid that hybridizes to the "STRA6 isoform 1" nucleic acid or its complement under low stringency conditions,

(lxxix) "Serine/threonine protein phosphatase 6" (SEQ ID No:90) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Serine/threonine protein phosphatase 6" encoded by a nucleic acid that hybridizes to the "Serine/threonine protein phosphatase 6" nucleic acid or its complement under low stringency conditions,

(lxxx) "Sortilin 1" (SEQ ID No:177) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sortilin 1" encoded by a nucleic acid that hybridizes to the "Sortilin 1" nucleic acid or its complement under low stringency conditions,

(lxxxi) "Stearoyl-CoA desaturase" (SEQ ID No:178) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Stearoyl-CoA desaturase" encoded by a nucleic acid that hybridizes to the "Stearoyl-CoA desaturase" nucleic acid or its complement under low stringency conditions,

(lxxxii) "Tparl" (SEQ ID No:179) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Tparl" encoded by a nucleic acid that hybridizes to the "Tparl" nucleic acid or its complement under low stringency conditions,

(lxxxiii) "Ubiquitin-protein ligase EDD" (SEQ ID No:180) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Ubiquitin-protein ligase EDD" encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase EDD" nucleic acid or its complement under low stringency conditions,

(lxxxiv) "Voltage-dependent anion channel 2" (SEQ ID No:181) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Voltage-dependent anion channel 2" encoded by a nucleic acid that hybridizes to the "Voltage-dependent anion channel 2" nucleic acid or its complement under low stringency conditions,

(lxxxv) "Wolframin" (SEQ ID No:182) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Wolframin" encoded by a nucleic acid that hybridizes to the "Wolframin" nucleic acid or its complement under low stringency conditions,

(lxxxvi) "cholinergic receptor, nicotinic, alpha polypeptide 3" (SEQ ID No:183) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "cholinergic receptor, nicotinic, alpha polypeptide 3" encoded by a nucleic acid that hybridizes to the "cholinergic receptor, nicotinic, alpha polypeptide 3" nucleic acid or its complement under low stringency conditions,

and/or(lxxxvii) "ensp00000297280 (hypothetical protein with p-loop)" (SEQ ID No:184) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ensp00000297280 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ensp00000297280 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions, as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

The present invention further relates to the following embodiments of the Nicastrin-complex:

1. A protein complex selected from complex (I) and comprising

(a) at least one first protein selected from the group consisting of:

(i) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,

(ii) "BACE1" (SEQ ID No:187) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BACE1" encoded by a nucleic acid that hybridizes to the "BACE1" nucleic acid or its complement under low stringency conditions,

(iii) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin"



encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,

(iv) "Pen-2" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions,

(v) "Presenilin-1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin-1" encoded by a nucleic acid that hybridizes to the "Presenilin-1" nucleic acid or its complement under low stringency conditions, and

(vi) "Presenilin-2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin-2" encoded by a nucleic acid that hybridizes to the "Presenilin-2" nucleic acid or its complement under low stringency conditions, and

(b) at least one second protein, which second protein is selected from the group consisting of:

(i) "18 kDa microsomal signal peptidase subunit" (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "18 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,

(ii) "25 kDa microsomal signal peptidase subunit" (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "25 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "25 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,

(iii) "ATP-binding cassette, sub-family A, member 3" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family A, member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A, member 3" nucleic acid or its complement under low stringency conditions,

(iv) "BSCv protein (FRAGMENT)" (SEQ ID No:188) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"BSCv protein (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "BSCv protein (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(v) "CAMK4" (SEQ ID No:189) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CAMK4" encoded by a nucleic acid that hybridizes to the "CAMK4" nucleic acid or its complement under low stringency conditions,

(vi) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,

(vii) "Casein kinase II beta chain" (SEQ ID No:190) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Casein kinase II beta chain" encoded by a nucleic acid that hybridizes to the "Casein kinase II beta chain" nucleic acid or its complement under low stringency conditions,

(viii) "Cathepsin B" (SEQ ID No:191) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cathepsin B" encoded by a nucleic acid that hybridizes to the "Cathepsin B" nucleic acid or its complement under low stringency conditions,

(ix) "DCTN1" (SEQ ID No:192) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DCTN1" encoded by a nucleic acid that hybridizes to the "DCTN1" nucleic acid or its complement under low stringency conditions,

(x) "Delta-6 fatty acid desaturase" (SEQ ID No:193) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-6 fatty acid desaturase" encoded by a nucleic acid that hybridizes to the "Delta-6 fatty acid desaturase" nucleic acid or its complement under low stringency conditions,

(xi) "ENSG00000144840" (SEQ ID No:194) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENSG00000144840" encoded by a nucleic acid that hybridizes to the "ENSG00000144840" nucleic acid or its complement under low stringency conditions,

(xii) "FACL3" (SEQ ID No:195) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FACL3" encoded by a nucleic acid that hybridizes to the "FACL3" nucleic acid or its complement under low stringency conditions,

- (xiii) "FACL4" (SEQ ID No:196) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FACL4" encoded by a nucleic acid that hybridizes to the "FACL4" nucleic acid or its complement under low stringency conditions,
- (xiv) "FLJ13977" (SEQ ID No:197) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13977" encoded by a nucleic acid that hybridizes to the "FLJ13977" nucleic acid or its complement under low stringency conditions,
- (xv) "FLJ20342" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions,
- (xvi) "FLJ20481" (SEQ ID No:198) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20481" encoded by a nucleic acid that hybridizes to the "FLJ20481" nucleic acid or its complement under low stringency conditions,
- (xvii) "FLJ22390" (SEQ ID No:199) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22390" encoded by a nucleic acid that hybridizes to the "FLJ22390" nucleic acid or its complement under low stringency conditions,
- (xviii) "ICAM-2" (SEQ ID No:200) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ICAM-2" encoded by a nucleic acid that hybridizes to the "ICAM-2" nucleic acid or its complement under low stringency conditions,
- (xix) "KIAA0095" (SEQ ID No:201) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0095" encoded by a nucleic acid that hybridizes to the "KIAA0095" nucleic acid or its complement under low stringency conditions,
- (xx) "KIAA0922" (SEQ ID No:202) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0922" encoded by a nucleic acid that hybridizes to the "KIAA0922" nucleic acid or its complement under low stringency conditions,
- (xxi) "KIAA1181 (FRAGMENT)" (SEQ ID No:203) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"KIAA1181 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1181 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xxii) "KIAA1533 (FRAGMENT)" (SEQ ID No:204) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1533 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1533 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xxiii) "Mesenchymal stem cell protein DSCD75" (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Mesenchymal stem cell protein DSCD75" encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75" nucleic acid or its complement under low stringency conditions,

(xxiv) "NICE-3" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions,

(xxv) "Neurotrypsin" (SEQ ID No:206) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions,

(xxvi) "PAS domain containing serine/threonine kinase" (SEQ ID No:207) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PAS domain containing serine/threonine kinase" encoded by a nucleic acid that hybridizes to the "PAS domain containing serine/threonine kinase" nucleic acid or its complement under low stringency conditions,

(xxvii) "PP1, regulatory subunit 15B" (SEQ ID No:208) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PP1, regulatory subunit 15B" encoded by a nucleic acid that hybridizes to the "PP1, regulatory subunit 15B" nucleic acid or its complement under low stringency conditions,

(xxviii) "Protein amplified in osteosarcoma (OS-9)" (SEQ ID No:211) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein amplified in osteosarcoma (OS-9)" encoded by a nucleic acid that hybridizes to the "Protein amplified in osteosarcoma (OS-9)" nucleic acid or its complement under low stringency conditions,

(xxix) "Protein similar to stromal cell-derived factor 2" (SEQ ID No:212) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to stromal cell-derived factor 2" encoded by a nucleic acid that hybridizes to the "Protein similar to stromal cell-derived factor 2" nucleic acid or its complement under low stringency conditions,

(xxx) "Protocadherin beta 8" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 8" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8" nucleic acid or its complement under low stringency conditions,

(xxxi) "REP8 protein" (SEQ ID No:214) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "REP8 protein" encoded by a nucleic acid that hybridizes to the "REP8 protein" nucleic acid or its complement under low stringency conditions,

(xxxii) "RING finger protein 5" (SEQ ID No:215) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RING finger protein 5" encoded by a nucleic acid that hybridizes to the "RING finger protein 5" nucleic acid or its complement under low stringency conditions,

(xxxiii) "Retinal short-chain dehydrogenase/reductase retSDR2" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2" encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2" nucleic acid or its complement under low stringency conditions,

(xxxiv) "Stromal cell-derived factor 2-like 1" (SEQ ID No:217) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Stromal cell-derived factor 2-like 1" encoded by a nucleic acid that hybridizes to the "Stromal cell-derived factor 2-like 1" nucleic acid or its complement under low stringency conditions,

(xxxv) "Thioredoxin domain-containing protein" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions,

(xxxvi) "homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)" (SEQ ID No:219) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)" encoded by a nucleic acid that hybridizes to the "homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)" nucleic acid or its complement under low stringency conditions, and

(xxxvii) "tyrosine phosphatase ensg00000149185" (SEQ ID No:220) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "tyrosine phosphatase ensg00000149185" encoded by a nucleic acid that hybridizes to the "tyrosine phosphatase ensg00000149185" nucleic acid or its complement under low stringency conditions, and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

2. The protein complex according to No. 1 wherein the first protein is the protein 'Nicastrin' (SEQ ID NO. 147), or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of 'Nicastrin' encoded by a nucleic acid that hybridizes to the 'Nicastrin' under low stringency conditions.

3. The protein complex according to No. 1 selected from complex (I) and comprising the following proteins:

(i) "18 kDa microsomal signal peptidase subunit" (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "18 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,

(ii) "25 kDa microsomal signal peptidase subunit" (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "25 kDa microsomal signal peptidase subunit" encoded by a nucleic acid

that hybridizes to the "25 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,

(iii) "ATP-binding cassette, sub-family A, member 3" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family A, member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A, member 3" nucleic acid or its complement under low stringency conditions,

(iv) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,

(v) "BACE1" (SEQ ID No:187) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BACE1" encoded by a nucleic acid that hybridizes to the "BACE1" nucleic acid or its complement under low stringency conditions,

(vi) "BSCv protein (FRAGMENT)" (SEQ ID No:188) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BSCv protein (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "BSCv protein (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(vii) "CAMK4" (SEQ ID No:189) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CAMK4" encoded by a nucleic acid that hybridizes to the "CAMK4" nucleic acid or its complement under low stringency conditions,

(viii) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,

(ix) "Casein kinase II beta chain" (SEQ ID No:190) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Casein kinase II beta chain" encoded by a nucleic acid that hybridizes to the "Casein kinase II beta chain" nucleic acid or its complement under low stringency conditions,

(x) "Cathepsin B" (SEQ ID No:191) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cathepsin B"

encoded by a nucleic acid that hybridizes to the "Cathepsin B" nucleic acid or its complement under low stringency conditions,

(xi) "DCTN1" (SEQ ID No:192) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DCTN1" encoded by a nucleic acid that hybridizes to the "DCTN1" nucleic acid or its complement under low stringency conditions,

(xii) "Delta-6 fatty acid desaturase" (SEQ ID No:193) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-6 fatty acid desaturase" encoded by a nucleic acid that hybridizes to the "Delta-6 fatty acid desaturase" nucleic acid or its complement under low stringency conditions,

(xiii) "ENSG00000144840" (SEQ ID No:194) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENSG00000144840" encoded by a nucleic acid that hybridizes to the "ENSG00000144840" nucleic acid or its complement under low stringency conditions,

(xiv) "FACL3" (SEQ ID No:195) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FACL3" encoded by a nucleic acid that hybridizes to the "FACL3" nucleic acid or its complement under low stringency conditions,

(xv) "FACL4" (SEQ ID No:196) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FACL4" encoded by a nucleic acid that hybridizes to the "FACL4" nucleic acid or its complement under low stringency conditions,

(xvi) "FLJ13977" (SEQ ID No:197) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13977" encoded by a nucleic acid that hybridizes to the "FLJ13977" nucleic acid or its complement under low stringency conditions,

(xvii) "FLJ20342" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions,

(xviii) "FLJ20481" (SEQ ID No:198) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20481" encoded by a nucleic acid that hybridizes to the "FLJ20481" nucleic acid or its complement under low stringency conditions,



- (xix) "FLJ22390" (SEQ ID No:199) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22390" encoded by a nucleic acid that hybridizes to the "FLJ22390" nucleic acid or its complement under low stringency conditions,
- (xx) "ICAM-2" (SEQ ID No:200) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ICAM-2" encoded by a nucleic acid that hybridizes to the "ICAM-2" nucleic acid or its complement under low stringency conditions,
- (xxi) "KIAA0095" (SEQ ID No:201) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0095" encoded by a nucleic acid that hybridizes to the "KIAA0095" nucleic acid or its complement under low stringency conditions,
- (xxii) "KIAA0922" (SEQ ID No:202) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0922" encoded by a nucleic acid that hybridizes to the "KIAA0922" nucleic acid or its complement under low stringency conditions,
- (xxiii) "KIAA1181 (FRAGMENT)" (SEQ ID No:203) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1181 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1181 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (xxiv) "KIAA1533 (FRAGMENT)" (SEQ ID No:204) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1533 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1533 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (xxv) "Mesenchymal stem cell protein DSCD75" (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Mesenchymal stem cell protein DSCD75" encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75" nucleic acid or its complement under low stringency conditions,
- (xxvi) "NICE-3" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions,

(xxvii) "Neurotrypsin" (SEQ ID No:206) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions,

(xxviii) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,

(xxix) "PAS domain containing serine/threonine kinase" (SEQ ID No:207) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PAS domain containing serine/threonine kinase" encoded by a nucleic acid that hybridizes to the "PAS domain containing serine/threonine kinase" nucleic acid or its complement under low stringency conditions,

(xxx) "PP1, regulatory subunit 15B" (SEQ ID No:208) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PP1, regulatory subunit 15B" encoded by a nucleic acid that hybridizes to the "PP1, regulatory subunit 15B" nucleic acid or its complement under low stringency conditions,

(xxxi) "Pen-2" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions,

(xxxii) "Presenilin-1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin-1" encoded by a nucleic acid that hybridizes to the "Presenilin-1" nucleic acid or its complement under low stringency conditions,

(xxxiii) "Presenilin-2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin-2" encoded by a nucleic acid that hybridizes to the "Presenilin-2" nucleic acid or its complement under low stringency conditions,

(xxxiv) "Protein amplified in osteosarcoma (OS-9)" (SEQ ID No:211) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein amplified in osteosarcoma (OS-9)" encoded by a nucleic acid that hybridizes to the "Protein amplified in osteosarcoma (OS-9)" nucleic acid or its complement under low stringency conditions,

(xxxv) "Protein similar to stromal cell-derived factor 2" (SEQ ID No:212) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to stromal cell-derived factor 2" encoded by a nucleic acid that hybridizes to the "Protein similar to stromal cell-derived factor 2" nucleic acid or its complement under low stringency conditions,

(xxxvi) "Protocadherin beta 8" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 8" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8" nucleic acid or its complement under low stringency conditions,

(xxxvii) "REP8 protein" (SEQ ID No:214) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "REP8 protein" encoded by a nucleic acid that hybridizes to the "REP8 protein" nucleic acid or its complement under low stringency conditions,

(xxxviii) "RING finger protein 5" (SEQ ID No:215) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RING finger protein 5" encoded by a nucleic acid that hybridizes to the "RING finger protein 5" nucleic acid or its complement under low stringency conditions,

(xxxix) "Retinal short-chain dehydrogenase/reductase retSDR2" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2" encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2" nucleic acid or its complement under low stringency conditions,

(xl) "Stromal cell-derived factor 2-like 1" (SEQ ID No:217) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Stromal cell-derived factor 2-like 1" encoded by a nucleic acid that hybridizes to the "Stromal cell-derived factor 2-like 1" nucleic acid or its complement under low stringency conditions,

(xli) "Thioredoxin domain-containing protein" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions,

(xlii) "homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)" (SEQ ID No:219) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)" encoded by a nucleic acid that hybridizes to the "homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)" nucleic acid or its complement under low stringency conditions, and/or

(xliii) "tyrosine phosphatase ensg00000149185" (SEQ ID No:220) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "tyrosine phosphatase ensg00000149185" encoded by a nucleic acid that hybridizes to the "tyrosine phosphatase ensg00000149185" nucleic acid or its complement under low stringency conditions,

and a protein complex selected from complex (II) and comprising the following proteins:

(i) "18 kDa microsomal signal peptidase subunit" (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "18 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,

(ii) "25 kDa microsomal signal peptidase subunit" (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "25 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "25 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,

(iii) "ATP-binding cassette, sub-family A, member 3" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family A, member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A, member 3" nucleic acid or its complement under low stringency conditions,

(iv) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,

(v) "BSCv protein (FRAGMENT)" (SEQ ID No:188) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"BSCv protein (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "BSCv protein (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(vi) "CAMK4" (SEQ ID No:189) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CAMK4" encoded by a nucleic acid that hybridizes to the "CAMK4" nucleic acid or its complement under low stringency conditions,

(vii) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,

(viii) "Casein kinase II beta chain" (SEQ ID No:190) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Casein kinase II beta chain" encoded by a nucleic acid that hybridizes to the "Casein kinase II beta chain" nucleic acid or its complement under low stringency conditions,

(ix) "Cathepsin B" (SEQ ID No:191) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cathepsin B" encoded by a nucleic acid that hybridizes to the "Cathepsin B" nucleic acid or its complement under low stringency conditions,

(x) "DCTN1" (SEQ ID No:192) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DCTN1" encoded by a nucleic acid that hybridizes to the "DCTN1" nucleic acid or its complement under low stringency conditions,

(xi) "Delta-6 fatty acid desaturase" (SEQ ID No:193) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-6 fatty acid desaturase" encoded by a nucleic acid that hybridizes to the "Delta-6 fatty acid desaturase" nucleic acid or its complement under low stringency conditions,

(xii) "ENSG00000144840" (SEQ ID No:194) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENSG00000144840" encoded by a nucleic acid that hybridizes to the "ENSG00000144840" nucleic acid or its complement under low stringency conditions,

(xiii) "FACL3" (SEQ ID No:195) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FACL3" encoded by a nucleic acid that hybridizes to the "FACL3" nucleic acid or its complement under low stringency conditions,

- (xiv) "FACL4" (SEQ ID No:196) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FACL4" encoded by a nucleic acid that hybridizes to the "FACL4" nucleic acid or its complement under low stringency conditions,
- (xv) "FLJ13977" (SEQ ID No:197) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13977" encoded by a nucleic acid that hybridizes to the "FLJ13977" nucleic acid or its complement under low stringency conditions,
- (xvi) "FLJ20342" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions,
- (xvii) "FLJ20481" (SEQ ID No:198) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20481" encoded by a nucleic acid that hybridizes to the "FLJ20481" nucleic acid or its complement under low stringency conditions,
- (xviii) "FLJ22390" (SEQ ID No:199) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22390" encoded by a nucleic acid that hybridizes to the "FLJ22390" nucleic acid or its complement under low stringency conditions,
- (xix) "ICAM-2" (SEQ ID No:200) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ICAM-2" encoded by a nucleic acid that hybridizes to the "ICAM-2" nucleic acid or its complement under low stringency conditions,
- (xx) "KIAA0095" (SEQ ID No:201) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0095" encoded by a nucleic acid that hybridizes to the "KIAA0095" nucleic acid or its complement under low stringency conditions,
- (xxi) "KIAA0922" (SEQ ID No:202) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0922" encoded by a nucleic acid that hybridizes to the "KIAA0922" nucleic acid or its complement under low stringency conditions,
- (xxii) "KIAA1181 (FRAGMENT)" (SEQ ID No:203) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"KIAA1181 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1181 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xxiii) "KIAA1533 (FRAGMENT)" (SEQ ID No:204) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1533 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1533 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xxiv) "Mesenchymal stem cell protein DSCD75" (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Mesenchymal stem cell protein DSCD75" encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75" nucleic acid or its complement under low stringency conditions,

(xxv) "NICE-3" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions,

(xxvi) "Neurotrypsin" (SEQ ID No:206) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions,

(xxvii) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,

(xxviii) "PAS domain containing serine/threonine kinase" (SEQ ID No:207) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PAS domain containing serine/threonine kinase" encoded by a nucleic acid that hybridizes to the "PAS domain containing serine/threonine kinase" nucleic acid or its complement under low stringency conditions,

(xxix) "PP1, regulatory subunit 15B" (SEQ ID No:208) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PP1, regulatory subunit 15B" encoded by a nucleic acid that hybridizes to the "PP1, regulatory subunit 15B" nucleic acid or its complement under low stringency conditions,

(xxx) "Presenilin-1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin-1"

encoded by a nucleic acid that hybridizes to the "Presenilin-1" nucleic acid or its complement under low stringency conditions,

(xxxi) "Presenilin-2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin-2" encoded by a nucleic acid that hybridizes to the "Presenilin-2" nucleic acid or its complement under low stringency conditions,

(xxxii) "Protein amplified in osteosarcoma (OS-9)" (SEQ ID No:211) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein amplified in osteosarcoma (OS-9)" encoded by a nucleic acid that hybridizes to the "Protein amplified in osteosarcoma (OS-9)" nucleic acid or its complement under low stringency conditions,

(xxxiii) "Protein similar to stromal cell-derived factor 2" (SEQ ID No:212) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to stromal cell-derived factor 2" encoded by a nucleic acid that hybridizes to the "Protein similar to stromal cell-derived factor 2" nucleic acid or its complement under low stringency conditions,

(xxxiv) "Protocadherin beta 8" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 8" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8" nucleic acid or its complement under low stringency conditions,

(xxxv) "REP8 protein" (SEQ ID No:214) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "REP8 protein" encoded by a nucleic acid that hybridizes to the "REP8 protein" nucleic acid or its complement under low stringency conditions,

(xxxvi) "RING finger protein 5" (SEQ ID No:215) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RING finger protein 5" encoded by a nucleic acid that hybridizes to the "RING finger protein 5" nucleic acid or its complement under low stringency conditions,

(xxxvii) "Retinal short-chain dehydrogenase/reductase retSDR2" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2" encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2" nucleic acid or its complement under low stringency conditions,



(xxxviii) "Stromal cell-derived factor 2-like 1" (SEQ ID No:217) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Stromal cell-derived factor 2-like 1" encoded by a nucleic acid that hybridizes to the "Stromal cell-derived factor 2-like 1" nucleic acid or its complement under low stringency conditions,

(xxxix) "Thioredoxin domain-containing protein" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions,

(xl) "homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)" (SEQ ID No:219) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)" encoded by a nucleic acid that hybridizes to the "homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)" nucleic acid or its complement under low stringency conditions, and/or

(xli) "tyrosine phosphatase ensg00000149185" (SEQ ID No:220) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "tyrosine phosphatase ensg00000149185" encoded by a nucleic acid that hybridizes to the "tyrosine phosphatase ensg00000149185" nucleic acid or its complement under low stringency conditions.

4. The protein complex according to No. 1 comprising all but 1 - 36 of the following proteins:

(i) "18 kDa microsomal signal peptidase subunit" (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "18 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,

(ii) "25 kDa microsomal signal peptidase subunit" (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "25 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "25 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,

- (iii) "ATP-binding cassette, sub-family A, member 3" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family A, member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A, member 3" nucleic acid or its complement under low stringency conditions,
- (iv) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,
- (v) "BACE1" (SEQ ID No:187) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BACE1" encoded by a nucleic acid that hybridizes to the "BACE1" nucleic acid or its complement under low stringency conditions,
- (vi) "BSCv protein (FRAGMENT)" (SEQ ID No:188) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BSCv protein (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "BSCv protein (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (vii) "CAMK4" (SEQ ID No:189) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CAMK4" encoded by a nucleic acid that hybridizes to the "CAMK4" nucleic acid or its complement under low stringency conditions,
- (viii) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,
- (ix) "Casein kinase II beta chain" (SEQ ID No:190) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Casein kinase II beta chain" encoded by a nucleic acid that hybridizes to the "Casein kinase II beta chain" nucleic acid or its complement under low stringency conditions,
- (x) "Cathepsin B" (SEQ ID No:191) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cathepsin B" encoded by a nucleic acid that hybridizes to the "Cathepsin B" nucleic acid or its complement under low stringency conditions,

- (xi) "DCTN1" (SEQ ID No:192) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DCTN1" encoded by a nucleic acid that hybridizes to the "DCTN1" nucleic acid or its complement under low stringency conditions,
- (xii) "Delta-6 fatty acid desaturase" (SEQ ID No:193) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-6 fatty acid desaturase" encoded by a nucleic acid that hybridizes to the "Delta-6 fatty acid desaturase" nucleic acid or its complement under low stringency conditions,
- (xiii) "ENSG00000144840" (SEQ ID No:194) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENSG00000144840" encoded by a nucleic acid that hybridizes to the "ENSG00000144840" nucleic acid or its complement under low stringency conditions,
- (xiv) "FACL3" (SEQ ID No:195) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FACL3" encoded by a nucleic acid that hybridizes to the "FACL3" nucleic acid or its complement under low stringency conditions,
- (xv) "FACL4" (SEQ ID No:196) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FACL4" encoded by a nucleic acid that hybridizes to the "FACL4" nucleic acid or its complement under low stringency conditions,
- (xvi) "FLJ13977" (SEQ ID No:197) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13977" encoded by a nucleic acid that hybridizes to the "FLJ13977" nucleic acid or its complement under low stringency conditions,
- (xvii) "FLJ20342" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions,
- (xviii) "FLJ20481" (SEQ ID No:198) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20481" encoded by a nucleic acid that hybridizes to the "FLJ20481" nucleic acid or its complement under low stringency conditions,
- (xix) "FLJ22390" (SEQ ID No:199) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22390"

encoded by a nucleic acid that hybridizes to the "FLJ22390" nucleic acid or its complement under low stringency conditions,

(xx) "ICAM-2" (SEQ ID No:200) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ICAM-2" encoded by a nucleic acid that hybridizes to the "ICAM-2" nucleic acid or its complement under low stringency conditions,

(xxi) "KIAA0095" (SEQ ID No:201) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0095" encoded by a nucleic acid that hybridizes to the "KIAA0095" nucleic acid or its complement under low stringency conditions,

(xxii) "KIAA0922" (SEQ ID No:202) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0922" encoded by a nucleic acid that hybridizes to the "KIAA0922" nucleic acid or its complement under low stringency conditions,

(xxiii) "KIAA1181 (FRAGMENT)" (SEQ ID No:203) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1181 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1181 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xxiv) "KIAA1533 (FRAGMENT)" (SEQ ID No:204) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1533 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1533 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xxv) "Mesenchymal stem cell protein DSCD75" (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Mesenchymal stem cell protein DSCD75" encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75" nucleic acid or its complement under low stringency conditions,

(xxvi) "NICE-3" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions,

(xxvii) "Neurotrypsin" (SEQ ID No:206) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin"

encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions,

(xxviii) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,

(xxix) "PAS domain containing serine/threonine kinase" (SEQ ID No:207) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PAS domain containing serine/threonine kinase" encoded by a nucleic acid that hybridizes to the "PAS domain containing serine/threonine kinase" nucleic acid or its complement under low stringency conditions,

(xxx) "PP1, regulatory subunit 15B" (SEQ ID No:208) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PP1, regulatory subunit 15B" encoded by a nucleic acid that hybridizes to the "PP1, regulatory subunit 15B" nucleic acid or its complement under low stringency conditions,

(xxxi) "Pen-2" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions,

(xxxii) "Presenilin-1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin-1" encoded by a nucleic acid that hybridizes to the "Presenilin-1" nucleic acid or its complement under low stringency conditions,

(xxxiii) "Presenilin-2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin-2" encoded by a nucleic acid that hybridizes to the "Presenilin-2" nucleic acid or its complement under low stringency conditions,

(xxxiv) "Protein amplified in osteosarcoma (OS-9)" (SEQ ID No:211) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein amplified in osteosarcoma (OS-9)" encoded by a nucleic acid that hybridizes to the "Protein amplified in osteosarcoma (OS-9)" nucleic acid or its complement under low stringency conditions,

(xxxv) "Protein similar to stromal cell-derived factor 2" (SEQ ID No:212) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof,

or a variant of "Protein similar to stromal cell-derived factor 2" encoded by a nucleic acid that hybridizes to the "Protein similar to stromal cell-derived factor 2" nucleic acid or its complement under low stringency conditions,

(xxxvi) "Protocadherin beta 8" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 8" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8" nucleic acid or its complement under low stringency conditions,

(xxxvii) "REP8 protein" (SEQ ID No:214) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "REP8 protein" encoded by a nucleic acid that hybridizes to the "REP8 protein" nucleic acid or its complement under low stringency conditions,

(xxxviii) "RING finger protein 5" (SEQ ID No:215) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RING finger protein 5" encoded by a nucleic acid that hybridizes to the "RING finger protein 5" nucleic acid or its complement under low stringency conditions,

(xxxix) "Retinal short-chain dehydrogenase/reductase retSDR2" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2" encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2" nucleic acid or its complement under low stringency conditions,

(xl) "Stromal cell-derived factor 2-like 1" (SEQ ID No:217) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Stromal cell-derived factor 2-like 1" encoded by a nucleic acid that hybridizes to the "Stromal cell-derived factor 2-like 1" nucleic acid or its complement under low stringency conditions,

(xli) "Thioredoxin domain-containing protein" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions,

(xlii) "homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)" (SEQ ID No:219) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "homolog of yeast golgi membrane protein

yif1p (yip1p-interacting factor)" encoded by a nucleic acid that hybridizes to the "homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)" nucleic acid or its complement under low stringency conditions,

(xlili) "tyrosine phosphatase ensg00000149185" (SEQ ID No:220) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "tyrosine phosphatase ensg00000149185" encoded by a nucleic acid that hybridizes to the "tyrosine phosphatase ensg00000149185" nucleic acid or its complement under low stringency conditions.

5. The complex of any of No. 1 - 4 comprising a functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein, respectively.

6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.

7. The complex of any of No. 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.

8. The complex of any of No. 1 - 7 that is involved in the the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by

modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)).

9. A process for preparing a complex of any of No. 1 - 8 and optionally the components thereof comprising the following steps: expressing a protein (bait) of the complex, preferably a tagged protein, in a target cell, isolating the protein complex which is attached to the bait protein, and optionally dissociating the protein complex and isolating the individual complex members.

10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.

11. The process according to any of No. 9 - 10 wherein the two tags are separated by a cleavage site for a protease.

12. Component of the Nicastrin complex obtainable by a process according to any of No. 9 - 11.

13. Protein of the Nicastrin complex selected from

(i) "ATP-binding cassette, sub-family A, member 3" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family A, member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A, member 3" nucleic acid or its complement under low stringency conditions,

(ii) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,

(iii) "ENSG00000144840" (SEQ ID No:194) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENSG00000144840" encoded by a nucleic acid that hybridizes to the "ENSG00000144840" nucleic acid or its complement under low stringency conditions,



- (iv) "FLJ20342" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions,
- (v) "FLJ20481" (SEQ ID No:198) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20481" encoded by a nucleic acid that hybridizes to the "FLJ20481" nucleic acid or its complement under low stringency conditions,
- (vi) "FLJ22390" (SEQ ID No:199) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22390" encoded by a nucleic acid that hybridizes to the "FLJ22390" nucleic acid or its complement under low stringency conditions,
- (vii) "KIAA0095" (SEQ ID No:201) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0095" encoded by a nucleic acid that hybridizes to the "KIAA0095" nucleic acid or its complement under low stringency conditions,
- (viii) "KIAA0922" (SEQ ID No:202) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0922" encoded by a nucleic acid that hybridizes to the "KIAA0922" nucleic acid or its complement under low stringency conditions,
- (ix) "KIAA1181 (FRAGMENT)" (SEQ ID No:203) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1181 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1181 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (x) "KIAA1533 (FRAGMENT)" (SEQ ID No:204) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1533 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1533 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (xi) "PP1, regulatory subunit 15B" (SEQ ID No:208) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PP1, regulatory subunit 15B" encoded by a nucleic acid that hybridizes to the "PP1, regulatory subunit 15B" nucleic acid or its complement under low stringency conditions,
- (xii) "RING finger protein 5" (SEQ ID No:215) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RING

finger protein 5" encoded by a nucleic acid that hybridizes to the "RING finger protein 5" nucleic acid or its complement under low stringency conditions,

(xiii) "Thioredoxin domain-containing protein" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions, and

(xiv) "tyrosine phosphatase ensg00000149185" (SEQ ID No:220) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "tyrosine phosphatase ensg00000149185" encoded by a nucleic acid that hybridizes to the "tyrosine phosphatase ensg00000149185" nucleic acid or its complement under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

14. Nucleic acid encoding a protein according to No. 13.

15. Construct, preferably a vector construct, comprising (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or

(b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative of at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the second group of proteins according to No. 1 (b).

16. Host cell, containing a vector comprising at least one of the nucleic acid of No. 14 and/or a construct of No. 15 or containing several vectors each comprising at least the

nucleic acid sequence encoding at least one of the proteins, or functionally active fragments or functionally active derivatives thereof selected from the first group of proteins according to No. 1 (a) and the proteins, or functionally active fragments or functionally active derivatives thereof selected from the second group of proteins according to No. 1 (b).

17. An antibody or a fragment of said antibody containing the binding domain thereof; selected from an antibody or fragment thereof, which binds the complex of any of No. 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody which binds to any of the proteins according to No. 13.

18. A kit comprising in one or more container the complex of any of No. 1 - 8 and/or the proteins of No. 13 optionally together with an antibody according to No. 17 and/or further components such as reagents and working instructions.

19. The kit according to No. 18 for processing a substrate of said complex.

20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

21. Array, in which at least a complex according to any of No. 1 - 8 and/or at least one protein according to No. 14 and/or at least one antibody according to No. 17 is attached to a solid carrier.

22. A process for processing a physiological substrate of the complex comprising the step of bringing into contact a complex to any of No. 1 - 8 with said substrate, such that said substrate is processed.

23. A pharmaceutical composition comprising the protein complex of any of No. 1 - 8 and/or any of the following the proteins:

(i) "ATP-binding cassette, sub-family A, member 3" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof,

or a variant of "ATP-binding cassette, sub-family A, member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A, member 3" nucleic acid or its complement under low stringency conditions,

(ii) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,

(iii) "ENSG00000144840" (SEQ ID No:194) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENSG00000144840" encoded by a nucleic acid that hybridizes to the "ENSG00000144840" nucleic acid or its complement under low stringency conditions,

(iv) "FLJ20342" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions,

(v) "FLJ20481" (SEQ ID No:198) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20481" encoded by a nucleic acid that hybridizes to the "FLJ20481" nucleic acid or its complement under low stringency conditions,

(vi) "FLJ22390" (SEQ ID No:199) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22390" encoded by a nucleic acid that hybridizes to the "FLJ22390" nucleic acid or its complement under low stringency conditions,

(vii) "KIAA0095" (SEQ ID No:201) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0095" encoded by a nucleic acid that hybridizes to the "KIAA0095" nucleic acid or its complement under low stringency conditions,

(viii) "KIAA0922" (SEQ ID No:202) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0922" encoded by a nucleic acid that hybridizes to the "KIAA0922" nucleic acid or its complement under low stringency conditions,

(ix) "KIAA1181 (FRAGMENT)" (SEQ ID No:203) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"KIAA1181 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1181 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(x) "KIAA1533 (FRAGMENT)" (SEQ ID No:204) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1533 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1533 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xi) "PP1, regulatory subunit 15B" (SEQ ID No:208) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PP1, regulatory subunit 15B" encoded by a nucleic acid that hybridizes to the "PP1, regulatory subunit 15B" nucleic acid or its complement under low stringency conditions,

(xii) "RING finger protein 5" (SEQ ID No:215) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RING finger protein 5" encoded by a nucleic acid that hybridizes to the "RING finger protein 5" nucleic acid or its complement under low stringency conditions,

(xiii) "Thioredoxin domain-containing protein" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions, and/or

(xiv) "tyrosine phosphatase ensg00000149185" (SEQ ID No:220) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "tyrosine phosphatase ensg00000149185" encoded by a nucleic acid that hybridizes to the "tyrosine phosphatase ensg00000149185" nucleic acid or its complement under low stringency conditions, and a pharmaceutical acceptable carrier.

24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

25. A method for screening for a molecule that binds to the complex of anyone of No. 1 - 8 and/or any of the following the proteins:

- (i) "ATP-binding cassette, sub-family A, member 3" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family A, member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A, member 3" nucleic acid or its complement under low stringency conditions,
- (ii) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,
- (iii) "ENSG00000144840" (SEQ ID No:194) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENSG00000144840" encoded by a nucleic acid that hybridizes to the "ENSG00000144840" nucleic acid or its complement under low stringency conditions,
- (iv) "FLJ20342" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions,
- (v) "FLJ20481" (SEQ ID No:198) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20481" encoded by a nucleic acid that hybridizes to the "FLJ20481" nucleic acid or its complement under low stringency conditions,
- (vi) "FLJ22390" (SEQ ID No:199) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22390" encoded by a nucleic acid that hybridizes to the "FLJ22390" nucleic acid or its complement under low stringency conditions,
- (vii) "KIAA0095" (SEQ ID No:201) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0095" encoded by a nucleic acid that hybridizes to the "KIAA0095" nucleic acid or its complement under low stringency conditions,
- (viii) "KIAA0922" (SEQ ID No:202) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0922" encoded by a nucleic acid that hybridizes to the "KIAA0922" nucleic acid or its complement under low stringency conditions,

- (ix) "KIAA1181 (FRAGMENT)" (SEQ ID No:203) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1181 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1181 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (x) "KIAA1533 (FRAGMENT)" (SEQ ID No:204) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1533 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1533 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (xi) "PP1, regulatory subunit 15B" (SEQ ID No:208) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PP1, regulatory subunit 15B" encoded by a nucleic acid that hybridizes to the "PP1, regulatory subunit 15B" nucleic acid or its complement under low stringency conditions,
- (xii) "RING finger protein 5" (SEQ ID No:215) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RING finger protein 5" encoded by a nucleic acid that hybridizes to the "RING finger protein 5" nucleic acid or its complement under low stringency conditions,
- (xiii) "Thioredoxin domain-containing protein" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions, and/or
- (xiv) "tyrosine phosphatase ensg00000149185" (SEQ ID No:220) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "tyrosine phosphatase ensg00000149185" encoded by a nucleic acid that hybridizes to the "tyrosine phosphatase ensg00000149185" nucleic acid or its complement under low stringency conditions, comprising the steps of
  - (a) exposing said complex, or a cell or organism containing same to one or more candidate molecules; and
  - (b) determining whether said candidate molecule is bound to the complex or protein.

26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 - 8 comprising the steps of (a) exposing said complex, or a cell or organism containing Nicastrin complex to one or more candidate molecules; and

(b) determining the amount of activity of protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.

27. The method of No. 26, wherein the amount of said complex is determined.

28. The method of No. 26, wherein the activity of said complex is determined.

29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining the processing of said substrate is modified in the presence of said candidate molecule.

30. The method of No. 26, wherein the amount of the individual protein components of said complex are determined.

31. The method of No. 30, wherein said determining step comprises determining whether

- (i) "18 kDa microsomal signal peptidase subunit" (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "18 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions, and/or
- (ii) "25 kDa microsomal signal peptidase subunit" (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof,



or a variant of "25 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "25 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions, and/or

(iii) "ATP-binding cassette, sub-family A, member 3" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family A, member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A, member 3" nucleic acid or its complement under low stringency conditions, and/or

(iv) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions, and/or

(v) "BACE1" (SEQ ID No:187) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BACE1" encoded by a nucleic acid that hybridizes to the "BACE1" nucleic acid or its complement under low stringency conditions, and/or

(vi) "BSCv protein (FRAGMENT)" (SEQ ID No:188) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BSCv protein (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "BSCv protein (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or

(vii) "CAMK4" (SEQ ID No:189) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CAMK4" encoded by a nucleic acid that hybridizes to the "CAMK4" nucleic acid or its complement under low stringency conditions, and/or

(viii) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions, and/or

(ix) "Casein kinase II beta chain" (SEQ ID No:190) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Casein kinase II beta chain" encoded by a nucleic acid that hybridizes to the "Casein kinase II beta chain" nucleic acid or its complement under low stringency conditions, and/or

- (x) "Cathepsin B" (SEQ ID No:191) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cathepsin B" encoded by a nucleic acid that hybridizes to the "Cathepsin B" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "DCTN1" (SEQ ID No:192) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DCTN1" encoded by a nucleic acid that hybridizes to the "DCTN1" nucleic acid or its complement under low stringency conditions, and/or
- (xii) "Delta-6 fatty acid desaturase" (SEQ ID No:193) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-6 fatty acid desaturase" encoded by a nucleic acid that hybridizes to the "Delta-6 fatty acid desaturase" nucleic acid or its complement under low stringency conditions, and/or
- (xiii) "ENSG00000144840" (SEQ ID No:194) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENSG00000144840" encoded by a nucleic acid that hybridizes to the "ENSG00000144840" nucleic acid or its complement under low stringency conditions, and/or
- (xiv) "FACL3" (SEQ ID No:195) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FACL3" encoded by a nucleic acid that hybridizes to the "FACL3" nucleic acid or its complement under low stringency conditions, and/or
- (xv) "FACL4" (SEQ ID No:196) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FACL4" encoded by a nucleic acid that hybridizes to the "FACL4" nucleic acid or its complement under low stringency conditions, and/or
- (xvi) "FLJ13977" (SEQ ID No:197) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13977" encoded by a nucleic acid that hybridizes to the "FLJ13977" nucleic acid or its complement under low stringency conditions, and/or
- (xvii) "FLJ20342" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions, and/or

- (xviii) "FLJ20481" (SEQ ID No:198) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20481" encoded by a nucleic acid that hybridizes to the "FLJ20481" nucleic acid or its complement under low stringency conditions, and/or
- (xix) "FLJ22390" (SEQ ID No:199) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22390" encoded by a nucleic acid that hybridizes to the "FLJ22390" nucleic acid or its complement under low stringency conditions, and/or
- (xx) "ICAM-2" (SEQ ID No:200) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ICAM-2" encoded by a nucleic acid that hybridizes to the "ICAM-2" nucleic acid or its complement under low stringency conditions, and/or
- (xxi) "KIAA0095" (SEQ ID No:201) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0095" encoded by a nucleic acid that hybridizes to the "KIAA0095" nucleic acid or its complement under low stringency conditions, and/or
- (xxii) "KIAA0922" (SEQ ID No:202) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0922" encoded by a nucleic acid that hybridizes to the "KIAA0922" nucleic acid or its complement under low stringency conditions, and/or
- (xxiii) "KIAA1181 (FRAGMENT)" (SEQ ID No:203) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1181 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1181 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or
- (xxiv) "KIAA1533 (FRAGMENT)" (SEQ ID No:204) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1533 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1533 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or
- (xxv) "Mesenchymal stem cell protein DSCD75" (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Mesenchymal stem cell protein DSCD75" encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75" nucleic acid or its complement under low stringency conditions, and/or

(xxvi) "NICE-3" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions, and/or

(xxvii) "Neurotrypsin" (SEQ ID No:206) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions, and/or

(xxviii) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions, and/or

(xxix) "PAS domain containing serine/threonine kinase" (SEQ ID No:207) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PAS domain containing serine/threonine kinase" encoded by a nucleic acid that hybridizes to the "PAS domain containing serine/threonine kinase" nucleic acid or its complement under low stringency conditions, and/or

(xxx) "PP1, regulatory subunit 15B" (SEQ ID No:208) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PP1, regulatory subunit 15B" encoded by a nucleic acid that hybridizes to the "PP1, regulatory subunit 15B" nucleic acid or its complement under low stringency conditions, and/or

(xxxi) "Pen-2" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions, and/or

(xxxii) "Presenilin-1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin-1" encoded by a nucleic acid that hybridizes to the "Presenilin-1" nucleic acid or its complement under low stringency conditions, and/or

(xxxiii) "Presenilin-2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin-2"

encoded by a nucleic acid that hybridizes to the "Presenilin-2" nucleic acid or its complement under low stringency conditions, and/or

(xxxiv) "Protein amplified in osteosarcoma (OS-9)" (SEQ ID No:211) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein amplified in osteosarcoma (OS-9)" encoded by a nucleic acid that hybridizes to the "Protein amplified in osteosarcoma (OS-9)" nucleic acid or its complement under low stringency conditions, and/or

(xxxv) "Protein similar to stromal cell-derived factor 2" (SEQ ID No:212) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to stromal cell-derived factor 2" encoded by a nucleic acid that hybridizes to the "Protein similar to stromal cell-derived factor 2" nucleic acid or its complement under low stringency conditions, and/or

(xxxvi) "Protocadherin beta 8" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 8" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8" nucleic acid or its complement under low stringency conditions, and/or

(xxxvii) "REP8 protein" (SEQ ID No:214) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "REP8 protein" encoded by a nucleic acid that hybridizes to the "REP8 protein" nucleic acid or its complement under low stringency conditions, and/or

(xxxviii) "RING finger protein 5" (SEQ ID No:215) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RING finger protein 5" encoded by a nucleic acid that hybridizes to the "RING finger protein 5" nucleic acid or its complement under low stringency conditions, and/or

(xxxix) "Retinal short-chain dehydrogenase/reductase retSDR2" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2" encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2" nucleic acid or its complement under low stringency conditions, and/or

(xl) "Stromal cell-derived factor 2-like 1" (SEQ ID No:217) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Stromal cell-derived factor 2-like 1" encoded by a nucleic acid that hybridizes

to the "Stromal cell-derived factor 2-like 1" nucleic acid or its complement under low stringency conditions, and/or

(xli) "Thioredoxin domain-containing protein" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions, and/or

(xlii) "homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)" (SEQ ID No:219) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)" encoded by a nucleic acid that hybridizes to the "homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)" nucleic acid or its complement under low stringency conditions, and/or

(xlili) "tyrosine phosphatase ensg00000149185" (SEQ ID No:220) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "tyrosine phosphatase ensg00000149185" encoded by a nucleic acid that hybridizes to the "tyrosine phosphatase ensg00000149185" nucleic acid or its complement under low stringency conditions, is present in the complex.

32. The method of any of No. 26 - 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 - 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

34. A method for the production of a pharmaceutical composition comprising carrying out the method of any of No. 1 - 8 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.

35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, activity of, or component composition of, or intracellular localization of the complex of any one of the No. 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in an analogous sample from a subject not having the disease or disorder or predisposition indicates the presence in the subject of the disease or disorder or predisposition in the subject.

36. The method of No. 35, wherein the amount of said complex is determined.

37. The method of No. 35, wherein the activity of said complex is determined.

38. The method of No. 37, wherein said determining step comprises isolating from the subject said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.

39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.

40. The method of No. 39, wherein said determining step comprises determining whether (i) "18 kDa microsomal signal peptidase subunit" (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "18 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions, and/or

- (ii) "25 kDa microsomal signal peptidase subunit" (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "25 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "25 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions, and/or
- (iii) "ATP-binding cassette, sub-family A, member 3" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family A, member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A, member 3" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions, and/or
- (v) "BACE1" (SEQ ID No:187) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BACE1" encoded by a nucleic acid that hybridizes to the "BACE1" nucleic acid or its complement under low stringency conditions, and/or
- (vi) "BSCv protein (FRAGMENT)" (SEQ ID No:188) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BSCv protein (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "BSCv protein (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or
- (vii) "CAMK4" (SEQ ID No:189) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CAMK4" encoded by a nucleic acid that hybridizes to the "CAMK4" nucleic acid or its complement under low stringency conditions, and/or
- (viii) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "Casein kinase II beta chain" (SEQ ID No:190) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Casein kinase II beta chain" encoded by a nucleic acid that hybridizes to the "Casein



kinase II beta chain" nucleic acid or its complement under low stringency conditions, and/or

(x) "Cathepsin B" (SEQ ID No:191) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cathepsin B" encoded by a nucleic acid that hybridizes to the "Cathepsin B" nucleic acid or its complement under low stringency conditions, and/or

(xi) "DCTN1" (SEQ ID No:192) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DCTN1" encoded by a nucleic acid that hybridizes to the "DCTN1" nucleic acid or its complement under low stringency conditions, and/or

(xii) "Delta-6 fatty acid desaturase" (SEQ ID No:193) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-6 fatty acid desaturase" encoded by a nucleic acid that hybridizes to the "Delta-6 fatty acid desaturase" nucleic acid or its complement under low stringency conditions, and/or

(xiii) "ENSG00000144840" (SEQ ID No:194) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENSG00000144840" encoded by a nucleic acid that hybridizes to the "ENSG00000144840" nucleic acid or its complement under low stringency conditions, and/or

(xiv) "FACL3" (SEQ ID No:195) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FACL3" encoded by a nucleic acid that hybridizes to the "FACL3" nucleic acid or its complement under low stringency conditions, and/or

(xv) "FACL4" (SEQ ID No:196) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FACL4" encoded by a nucleic acid that hybridizes to the "FACL4" nucleic acid or its complement under low stringency conditions, and/or

(xvi) "FLJ13977" (SEQ ID No:197) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13977" encoded by a nucleic acid that hybridizes to the "FLJ13977" nucleic acid or its complement under low stringency conditions, and/or

(xvii) "FLJ20342" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20342"

encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions, and/or

(xviii) "FLJ20481" (SEQ ID No:198) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20481" encoded by a nucleic acid that hybridizes to the "FLJ20481" nucleic acid or its complement under low stringency conditions, and/or

(xix) "FLJ22390" (SEQ ID No:199) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22390" encoded by a nucleic acid that hybridizes to the "FLJ22390" nucleic acid or its complement under low stringency conditions, and/or

(xx) "ICAM-2" (SEQ ID No:200) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ICAM-2" encoded by a nucleic acid that hybridizes to the "ICAM-2" nucleic acid or its complement under low stringency conditions, and/or

(xxi) "KIAA0095" (SEQ ID No:201) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0095" encoded by a nucleic acid that hybridizes to the "KIAA0095" nucleic acid or its complement under low stringency conditions, and/or

(xxii) "KIAA0922" (SEQ ID No:202) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0922" encoded by a nucleic acid that hybridizes to the "KIAA0922" nucleic acid or its complement under low stringency conditions, and/or

(xxiii) "KIAA1181 (FRAGMENT)" (SEQ ID No:203) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1181 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1181 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or

(xxiv) "KIAA1533 (FRAGMENT)" (SEQ ID No:204) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1533 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1533 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or

(xxv) "Mesenchymal stem cell protein DSCD75" (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Mesenchymal stem cell protein DSCD75" encoded by a nucleic acid that

hybridizes to the "Mesenchymal stem cell protein DSCD75" nucleic acid or its complement under low stringency conditions, and/or

(xxvi) "NICE-3" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions, and/or

(xxvii) "Neurotrypsin" (SEQ ID No:206) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions, and/or

(xxviii) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions, and/or

(xxix) "PAS domain containing serine/threonine kinase" (SEQ ID No:207) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PAS domain containing serine/threonine kinase" encoded by a nucleic acid that hybridizes to the "PAS domain containing serine/threonine kinase" nucleic acid or its complement under low stringency conditions, and/or

(xxx) "PP1, regulatory subunit 15B" (SEQ ID No:208) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PP1, regulatory subunit 15B" encoded by a nucleic acid that hybridizes to the "PP1, regulatory subunit 15B" nucleic acid or its complement under low stringency conditions, and/or

(xxxi) "Pen-2" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions, and/or

(xxxii) "Presenilin-1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin-1" encoded by a nucleic acid that hybridizes to the "Presenilin-1" nucleic acid or its complement under low stringency conditions, and/or

- (xxxiii) "Presenilin-2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin-2" encoded by a nucleic acid that hybridizes to the "Presenilin-2" nucleic acid or its complement under low stringency conditions, and/or
- (xxxiv) "Protein amplified in osteosarcoma (OS-9)" (SEQ ID No:211) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein amplified in osteosarcoma (OS-9)" encoded by a nucleic acid that hybridizes to the "Protein amplified in osteosarcoma (OS-9)" nucleic acid or its complement under low stringency conditions, and/or
- (xxxv) "Protein similar to stromal cell-derived factor 2" (SEQ ID No:212) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to stromal cell-derived factor 2" encoded by a nucleic acid that hybridizes to the "Protein similar to stromal cell-derived factor 2" nucleic acid or its complement under low stringency conditions, and/or
- (xxxvi) "Protocadherin beta 8" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 8" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8" nucleic acid or its complement under low stringency conditions, and/or
- (xxxvii) "REP8 protein" (SEQ ID No:214) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "REP8 protein" encoded by a nucleic acid that hybridizes to the "REP8 protein" nucleic acid or its complement under low stringency conditions, and/or
- (xxxviii) "RING finger protein 5" (SEQ ID No:215) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RING finger protein 5" encoded by a nucleic acid that hybridizes to the "RING finger protein 5" nucleic acid or its complement under low stringency conditions, and/or
- (xxxix) "Retinal short-chain dehydrogenase/reductase retSDR2" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2" encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "Stromal cell-derived factor 2-like 1" (SEQ ID No:217) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a

variant of "Stromal cell-derived factor 2-like 1" encoded by a nucleic acid that hybridizes to the "Stromal cell-derived factor 2-like 1" nucleic acid or its complement under low stringency conditions, and/or

(xli) "Thioredoxin domain-containing protein" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions, and/or

(xlii) "homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)" (SEQ ID No:219) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)" encoded by a nucleic acid that hybridizes to the "homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)" nucleic acid or its complement under low stringency conditions, and/or

(xlili) "tyrosine phosphatase ensg00000149185" (SEQ ID No:220) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "tyrosine phosphatase ensg00000149185" encoded by a nucleic acid that hybridizes to the "tyrosine phosphatase ensg00000149185" nucleic acid or its complement under low stringency conditions, is present in the complex.

41. The complex of any one of No. 1 - 8, or proteins of No. 13 or the antibody or fragment of No. 17, for use in a method of diagnosing a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity or component composition of or intracellular localization of, the complex of anyone of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by

modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), or protein components of, said complex.

43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.

44. The method according to No. 42, wherein said disease or disorder involves increased levels of the amount or activity of said complex.

45. Complex of any of No. 1 - 8 and/or protein selected from the following proteins

(i) "18 kDa microsomal signal peptidase subunit" (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "18 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,

(ii) "25 kDa microsomal signal peptidase subunit" (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "25 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "25 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,

(iii) "ATP-binding cassette, sub-family A, member 3" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family A, member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A, member 3" nucleic acid or its complement under low stringency conditions,

(iv) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a

nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,

(v) "BACE1" (SEQ ID No:187) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BACE1" encoded by a nucleic acid that hybridizes to the "BACE1" nucleic acid or its complement under low stringency conditions,

(vi) "BSCv protein (FRAGMENT)" (SEQ ID No:188) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BSCv protein (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "BSCv protein (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(vii) "CAMK4" (SEQ ID No:189) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CAMK4" encoded by a nucleic acid that hybridizes to the "CAMK4" nucleic acid or its complement under low stringency conditions,

(viii) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,

(ix) "Casein kinase II beta chain" (SEQ ID No:190) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Casein kinase II beta chain" encoded by a nucleic acid that hybridizes to the "Casein kinase II beta chain" nucleic acid or its complement under low stringency conditions,

(x) "Cathepsin B" (SEQ ID No:191) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cathepsin B" encoded by a nucleic acid that hybridizes to the "Cathepsin B" nucleic acid or its complement under low stringency conditions,

(xi) "DCTN1" (SEQ ID No:192) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DCTN1" encoded by a nucleic acid that hybridizes to the "DCTN1" nucleic acid or its complement under low stringency conditions,

(xii) "Delta-6 fatty acid desaturase" (SEQ ID No:193) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-6 fatty acid desaturase" encoded by a nucleic acid that hybridizes to the "Delta-6 fatty acid desaturase" nucleic acid or its complement under low stringency conditions,

- (xiii) "ENSG00000144840" (SEQ ID No:194) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENSG00000144840" encoded by a nucleic acid that hybridizes to the "ENSG00000144840" nucleic acid or its complement under low stringency conditions,
- (xiv) "FACL3" (SEQ ID No:195) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FACL3" encoded by a nucleic acid that hybridizes to the "FACL3" nucleic acid or its complement under low stringency conditions,
- (xv) "FACL4" (SEQ ID No:196) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FACL4" encoded by a nucleic acid that hybridizes to the "FACL4" nucleic acid or its complement under low stringency conditions,
- (xvi) "FLJ13977" (SEQ ID No:197) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13977" encoded by a nucleic acid that hybridizes to the "FLJ13977" nucleic acid or its complement under low stringency conditions,
- (xvii) "FLJ20342" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions,
- (xviii) "FLJ20481" (SEQ ID No:198) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20481" encoded by a nucleic acid that hybridizes to the "FLJ20481" nucleic acid or its complement under low stringency conditions,
- (xix) "FLJ22390" (SEQ ID No:199) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22390" encoded by a nucleic acid that hybridizes to the "FLJ22390" nucleic acid or its complement under low stringency conditions,
- (xx) "ICAM-2" (SEQ ID No:200) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ICAM-2" encoded by a nucleic acid that hybridizes to the "ICAM-2" nucleic acid or its complement under low stringency conditions,
- (xxi) "KIAA0095" (SEQ ID No:201) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0095"



encoded by a nucleic acid that hybridizes to the "KIAA0095" nucleic acid or its complement under low stringency conditions,

(xxii) "KIAA0922" (SEQ ID No:202) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0922" encoded by a nucleic acid that hybridizes to the "KIAA0922" nucleic acid or its complement under low stringency conditions,

(xxiii) "KIAA1181 (FRAGMENT)" (SEQ ID No:203) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1181 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1181 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xxiv) "KIAA1533 (FRAGMENT)" (SEQ ID No:204) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1533 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1533 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xxv) "Mesenchymal stem cell protein DSCD75" (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Mesenchymal stem cell protein DSCD75" encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75" nucleic acid or its complement under low stringency conditions,

(xxvi) "NICE-3" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions,

(xxvii) "Neurotrypsin" (SEQ ID No:206) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions,

(xxviii) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,

(xxix) "PAS domain containing serine/threonine kinase" (SEQ ID No:207) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PAS domain containing serine/threonine kinase"

encoded by a nucleic acid that hybridizes to the "PAS domain containing serine/threonine kinase" nucleic acid or its complement under low stringency conditions,

(xxx) "PP1, regulatory subunit 15B" (SEQ ID No:208) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PP1, regulatory subunit 15B" encoded by a nucleic acid that hybridizes to the "PP1, regulatory subunit 15B" nucleic acid or its complement under low stringency conditions,

(xxxi) "Pen-2" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions,

(xxxii) "Presenilin-1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin-1" encoded by a nucleic acid that hybridizes to the "Presenilin-1" nucleic acid or its complement under low stringency conditions,

(xxxiii) "Presenilin-2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin-2" encoded by a nucleic acid that hybridizes to the "Presenilin-2" nucleic acid or its complement under low stringency conditions,

(xxxiv) "Protein amplified in osteosarcoma (OS-9)" (SEQ ID No:211) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein amplified in osteosarcoma (OS-9)" encoded by a nucleic acid that hybridizes to the "Protein amplified in osteosarcoma (OS-9)" nucleic acid or its complement under low stringency conditions,

(xxxv) "Protein similar to stromal cell-derived factor 2" (SEQ ID No:212) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to stromal cell-derived factor 2" encoded by a nucleic acid that hybridizes to the "Protein similar to stromal cell-derived factor 2" nucleic acid or its complement under low stringency conditions,

(xxxvi) "Protocadherin beta 8" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 8" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8" nucleic acid or its complement under low stringency conditions,

(xxxvii) "REP8 protein" (SEQ ID No:214) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "REP8 protein"

encoded by a nucleic acid that hybridizes to the "REP8 protein" nucleic acid or its complement under low stringency conditions,

(xxxviii) "RING finger protein 5" (SEQ ID No:215) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RING finger protein 5" encoded by a nucleic acid that hybridizes to the "RING finger protein 5" nucleic acid or its complement under low stringency conditions,

(xxxix) "Retinal short-chain dehydrogenase/reductase retSDR2" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2" encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2" nucleic acid or its complement under low stringency conditions,

(xi) "Stromal cell-derived factor 2-like 1" (SEQ ID No:217) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Stromal cell-derived factor 2-like 1" encoded by a nucleic acid that hybridizes to the "Stromal cell-derived factor 2-like 1" nucleic acid or its complement under low stringency conditions,

(xli) "Thioredoxin domain-containing protein" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions,

(xlii) "homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)" (SEQ ID No:219) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)" encoded by a nucleic acid that hybridizes to the "homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)" nucleic acid or its complement under low stringency conditions, and/or(xliii) "tyrosine phosphatase ensg00000149185" (SEQ ID No:220) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "tyrosine phosphatase ensg00000149185" encoded by a nucleic acid that hybridizes to the "tyrosine phosphatase ensg00000149185" nucleic acid or its complement under low stringency conditions,as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder such as

neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

The present invention further relates to the following embodiments of the Aph1a-complex

1. A protein complex selected from complex (I) and comprising
  - (a) at least one first protein selected from the group consisting of:
    - (i) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,
    - (ii) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,
    - (iii) "Pen-2" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions,
    - (iv) "Presenilin 1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions, and
    - (v) "Presenilin 2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions, and
  - (b) at least one second protein, which second protein is selected from the group consisting of:
    - (i) "18 kDa microsomal signal peptidase subunit " (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "18 kDa microsomal signal peptidase subunit " encoded by a nucleic acid

that hybridizes to the "18 kDa microsomal signal peptidase subunit " nucleic acid or its complement under low stringency conditions,

(ii) "23 kDa microsomal signal peptidase" (SEQ ID No:221) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "23 kDa microsomal signal peptidase" encoded by a nucleic acid that hybridizes to the "23 kDa microsomal signal peptidase" nucleic acid or its complement under low stringency conditions,

(iii) "25 kDa microsomal signal peptidase subunit" (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "25 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "25 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,

(iv) "ABCC1" (SEQ ID No:222) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ABCC1" encoded by a nucleic acid that hybridizes to the "ABCC1" nucleic acid or its complement under low stringency conditions,

(v) "APLP2" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions,

(vi) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,

(vii) "ATM" (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATM" encoded by a nucleic acid that hybridizes to the "ATM" nucleic acid or its complement under low stringency conditions,

(viii) "ATP-binding cassette, sub-family A member 3" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family A member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A member 3" nucleic acid or its complement under low stringency conditions,

- (ix) "ATP1B1" (SEQ ID No:223) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP1B1" encoded by a nucleic acid that hybridizes to the "ATP1B1" nucleic acid or its complement under low stringency conditions,
- (x) "ATP2C1" (SEQ ID No:224) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP2C1" encoded by a nucleic acid that hybridizes to the "ATP2C1" nucleic acid or its complement under low stringency conditions,
- (xi) "Acetolactate synthase homolog" (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Acetolactate synthase homolog" encoded by a nucleic acid that hybridizes to the "Acetolactate synthase homolog" nucleic acid or its complement under low stringency conditions,
- (xii) "Brain-specific GTP-binding protein" (SEQ ID No:225) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Brain-specific GTP-binding protein" encoded by a nucleic acid that hybridizes to the "Brain-specific GTP-binding protein" nucleic acid or its complement under low stringency conditions,
- (xiii) "CDW92" (SEQ ID No:226) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDW92" encoded by a nucleic acid that hybridizes to the "CDW92" nucleic acid or its complement under low stringency conditions,
- (xiv) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,
- (xv) "CNTNAP1" (SEQ ID No:227) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CNTNAP1" encoded by a nucleic acid that hybridizes to the "CNTNAP1" nucleic acid or its complement under low stringency conditions,
- (xvi) "Cerebral protein-10" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cerebral protein-10" encoded by a nucleic acid that hybridizes to the "Cerebral protein-10" nucleic acid or its complement under low stringency conditions,

- (xvii) "DNM1" (SEQ ID No:228) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DNM1" encoded by a nucleic acid that hybridizes to the "DNM1" nucleic acid or its complement under low stringency conditions,
- (xviii) "Dihydrofolate reductase" (SEQ ID No:229) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dihydrofolate reductase" encoded by a nucleic acid that hybridizes to the "Dihydrofolate reductase" nucleic acid or its complement under low stringency conditions,
- (xix) "ENG" (SEQ ID No:230) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENG" encoded by a nucleic acid that hybridizes to the "ENG" nucleic acid or its complement under low stringency conditions,
- (xx) "EXT2" (SEQ ID No:231) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EXT2" encoded by a nucleic acid that hybridizes to the "EXT2" nucleic acid or its complement under low stringency conditions,
- (xxi) "EXTL3" (SEQ ID No:232) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EXTL3" encoded by a nucleic acid that hybridizes to the "EXTL3" nucleic acid or its complement under low stringency conditions,
- (xxii) "Endocytic receptor Endo180" (SEQ ID No:233) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Endocytic receptor Endo180" encoded by a nucleic acid that hybridizes to the "Endocytic receptor Endo180" nucleic acid or its complement under low stringency conditions,
- (xxiii) "FLJ13660" (SEQ ID No:234) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13660" encoded by a nucleic acid that hybridizes to the "FLJ13660" nucleic acid or its complement under low stringency conditions,
- (xxiv) "GPR49" (SEQ ID No:235) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GPR49" encoded by a nucleic acid that hybridizes to the "GPR49" nucleic acid or its complement under low stringency conditions,

(xxv) "HK2" (SEQ ID No:236) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HK2" encoded by a nucleic acid that hybridizes to the "HK2" nucleic acid or its complement under low stringency conditions,

(xxvi) "HU-K4" (SEQ ID No:133) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HU-K4" encoded by a nucleic acid that hybridizes to the "HU-K4" nucleic acid or its complement under low stringency conditions,

(xxvii) "HUNC18a" (SEQ ID No:54) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HUNC18a" encoded by a nucleic acid that hybridizes to the "HUNC18a" nucleic acid or its complement under low stringency conditions,

(xxviii) "HYPOTHETICAL PROTEIN " (SEQ ID No:237) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN " encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN " nucleic acid or its complement under low stringency conditions,

(xxix) "Hypothetical protein (Fragment)" (SEQ ID No:238) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein (Fragment)" encoded by a nucleic acid that hybridizes to the "Hypothetical protein (Fragment)" nucleic acid or its complement under low stringency conditions,

(xxx) "Hypothetical protein FLJ14562" (SEQ ID No:239) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ14562" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ14562" nucleic acid or its complement under low stringency conditions,

(xxxi) "Hypothetical protein FLJ23630" (SEQ ID No:240) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ23630" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ23630" nucleic acid or its complement under low stringency conditions,

(xxxii) "Hypothetical protein KIAA0372" (SEQ ID No:241) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a



variant of "Hypothetical protein KIAA0372" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0372" nucleic acid or its complement under low stringency conditions,

(xxxiii) "ICAM2" (SEQ ID No:200) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ICAM2" encoded by a nucleic acid that hybridizes to the "ICAM2" nucleic acid or its complement under low stringency conditions,

(xxxiv) "IGF2R" (SEQ ID No:242) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IGF2R" encoded by a nucleic acid that hybridizes to the "IGF2R" nucleic acid or its complement under low stringency conditions,

(xxxv) "ITPR1" (SEQ ID No:243) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITPR1" encoded by a nucleic acid that hybridizes to the "ITPR1" nucleic acid or its complement under low stringency conditions,

(xxxvi) "Insulinoma-glucagonoma protein 20" (SEQ ID No:58) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Insulinoma-glucagonoma protein 20" encoded by a nucleic acid that hybridizes to the "Insulinoma-glucagonoma protein 20" nucleic acid or its complement under low stringency conditions,

(xxxvii) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions,

(xxxviii) "KIAA0062 (FRAGMENT)" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0062 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0062 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xxxix) "KIAA0251 (FRAGMENT)" (SEQ ID No:244) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0251 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0251 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

- (xi) "KIAA0363 (FRAGMENT)" (SEQ ID No:245) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0363 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0363 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (xli) "KIAA0763" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions,
- (xlii) "KIAA0971" (SEQ ID No:246) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0971" encoded by a nucleic acid that hybridizes to the "KIAA0971" nucleic acid or its complement under low stringency conditions,
- (xliii) "KIAA1250" (SEQ ID No:247) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1250" encoded by a nucleic acid that hybridizes to the "KIAA1250" nucleic acid or its complement under low stringency conditions,
- (xliv) "LRP5" (SEQ ID No:248) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LRP5" encoded by a nucleic acid that hybridizes to the "LRP5" nucleic acid or its complement under low stringency conditions,
- (xlv) "MGC4248 " (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4248 " encoded by a nucleic acid that hybridizes to the "MGC4248 " nucleic acid or its complement under low stringency conditions,
- (xlvi) "Mesenchymal stem cell protein DSCD75" (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Mesenchymal stem cell protein DSCD75" encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75" nucleic acid or its complement under low stringency conditions,
- (xlvii) "NRP2" (SEQ ID No:249) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NRP2" encoded by a nucleic acid that hybridizes to the "NRP2" nucleic acid or its complement under low stringency conditions,

(xlvi) "Neurotrypsin" (SEQ ID No:206) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions,

(xlix) "PCDHA10" (SEQ ID No:250) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHA10" encoded by a nucleic acid that hybridizes to the "PCDHA10" nucleic acid or its complement under low stringency conditions,

(l) "PCDHB12" (SEQ ID No:251) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB12" encoded by a nucleic acid that hybridizes to the "PCDHB12" nucleic acid or its complement under low stringency conditions,

(li) "PCDHB13: protocadherin beta 13" (SEQ ID No:252) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB13: protocadherin beta 13" encoded by a nucleic acid that hybridizes to the "PCDHB13: protocadherin beta 13" nucleic acid or its complement under low stringency conditions,

(lii) "PCDHB4" (SEQ ID No:253) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB4" encoded by a nucleic acid that hybridizes to the "PCDHB4" nucleic acid or its complement under low stringency conditions,

(liii) "PCDHGB1" (SEQ ID No:254) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHGB1" encoded by a nucleic acid that hybridizes to the "PCDHGB1" nucleic acid or its complement under low stringency conditions,

(liv) "PCDHGB6" (SEQ ID No:255) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHGB6" encoded by a nucleic acid that hybridizes to the "PCDHGB6" nucleic acid or its complement under low stringency conditions,

(lv) "PMPCB" (SEQ ID No:256) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PMPCB" encoded by a nucleic acid that hybridizes to the "PMPCB" nucleic acid or its complement under low stringency conditions,

- (lvi) "PP2C gamma" (SEQ ID No:257) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PP2C gamma" encoded by a nucleic acid that hybridizes to the "PP2C gamma" nucleic acid or its complement under low stringency conditions,
- (lvii) "Pcdhb17" (SEQ ID No:258) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pcdhb17" encoded by a nucleic acid that hybridizes to the "Pcdhb17" nucleic acid or its complement under low stringency conditions,
- (lviii) "Protocadherin 7" (SEQ ID No:259) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin 7" encoded by a nucleic acid that hybridizes to the "Protocadherin 7" nucleic acid or its complement under low stringency conditions,
- (lix) "Protocadherin beta 16" (SEQ ID No:260) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 16" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 16" nucleic acid or its complement under low stringency conditions,
- (lx) "Protocadherin beta 8" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 8" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8" nucleic acid or its complement under low stringency conditions,
- (lxi) "RAB-18" (SEQ ID No:261) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB-18" encoded by a nucleic acid that hybridizes to the "RAB-18" nucleic acid or its complement under low stringency conditions,
- (lxii) "RNASEL" (SEQ ID No:262) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RNASEL" encoded by a nucleic acid that hybridizes to the "RNASEL" nucleic acid or its complement under low stringency conditions,
- (lxiii) "Rab3 GTPase-activating protein, non-catalytic subunit" (SEQ ID No:263) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Rab3 GTPase-activating protein, non-catalytic subunit" encoded by a nucleic acid that hybridizes to the "Rab3 GTPase-activating protein, non-catalytic subunit" nucleic acid or its complement under low stringency conditions,

(lxiv) "Retinal short-chain dehydrogenase/reductase retSDR2" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2" encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2" nucleic acid or its complement under low stringency conditions,

(lxv) "SMAP-1B" (SEQ ID No:264) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SMAP-1B" encoded by a nucleic acid that hybridizes to the "SMAP-1B" nucleic acid or its complement under low stringency conditions,

(lxvi) "SPTLC2" (SEQ ID No:265) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SPTLC2" encoded by a nucleic acid that hybridizes to the "SPTLC2" nucleic acid or its complement under low stringency conditions,

(lxvii) "STMN3" (SEQ ID No:87) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STMN3" encoded by a nucleic acid that hybridizes to the "STMN3" nucleic acid or its complement under low stringency conditions,

(lxviii) "Sideroflexin 1" (SEQ ID No:266) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sideroflexin 1" encoded by a nucleic acid that hybridizes to the "Sideroflexin 1" nucleic acid or its complement under low stringency conditions,

(lxix) "Signal transducer and activator of transcription-1" (SEQ ID No:267) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Signal transducer and activator of transcription-1" encoded by a nucleic acid that hybridizes to the "Signal transducer and activator of transcription-1" nucleic acid or its complement under low stringency conditions,

(lxx) "Similar to CGI-135 protein" (SEQ ID No:268) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to CGI-135 protein" encoded by a nucleic acid that hybridizes to the "Similar to CGI-135 protein" nucleic acid or its complement under low stringency conditions,

(lxxi) "Sterile alpha and HEAT/Armadillo motif protein" (SEQ ID No:269) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sterile alpha and HEAT/Armadillo motif protein" encoded by a nucleic

acid that hybridizes to the "Sterile alpha and HEAT/Armadillo motif protein" nucleic acid or its complement under low stringency conditions,

(lxxii) "Sterol O-acyltransferase 1" (SEQ ID No:270) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sterol O-acyltransferase 1" encoded by a nucleic acid that hybridizes to the "Sterol O-acyltransferase 1" nucleic acid or its complement under low stringency conditions,

(lxxiii) "Thioredoxin domain-containing protein" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions,

(lxxiv) "Triple functional domain protein (PTPRF interacting)" (SEQ ID No:271) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Triple functional domain protein (PTPRF interacting)" encoded by a nucleic acid that hybridizes to the "Triple functional domain protein (PTPRF interacting)" nucleic acid or its complement under low stringency conditions,

(lxxv) "UNC5C" (SEQ ID No:272) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "UNC5C" encoded by a nucleic acid that hybridizes to the "UNC5C" nucleic acid or its complement under low stringency conditions,

(lxxvi) "Vacuolar ATP synthase membrane sector associated protein m8-9" (SEQ ID No:273) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Vacuolar ATP synthase membrane sector associated protein m8-9" encoded by a nucleic acid that hybridizes to the "Vacuolar ATP synthase membrane sector associated protein m8-9" nucleic acid or its complement under low stringency conditions,

(lxxvii) "Y391\_HUMAN" (SEQ ID No:274) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Y391\_HUMAN" encoded by a nucleic acid that hybridizes to the "Y391\_HUMAN" nucleic acid or its complement under low stringency conditions,

(lxxviii) "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" (SEQ ID No:275) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" encoded by a nucleic acid that hybridizes to the

"hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" nucleic acid or its complement under low stringency conditions,

(lxxix) "hypothetical protein MGC22916" (SEQ ID No:276) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC22916" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC22916" nucleic acid or its complement under low stringency conditions,

(lxxx) "integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "integral membrane transporter protein" nucleic acid or its complement under low stringency conditions,

(lxxxi) "tegt: testis enhanced gene transcript (bax inhibitor 1)" (SEQ ID No:278) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "tegt: testis enhanced gene transcript (bax inhibitor 1)" encoded by a nucleic acid that hybridizes to the "tegt: testis enhanced gene transcript (bax inhibitor 1)" nucleic acid or its complement under low stringency conditions, and (lxxxii) "vacuolar protein sorting protein 18" (SEQ ID No:279) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "vacuolar protein sorting protein 18" encoded by a nucleic acid that hybridizes to the "vacuolar protein sorting protein 18" nucleic acid or its complement under low stringency conditions, and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

2. The protein complex according to No. 1 wherein the first protein is the protein 'Aph1a' (SEQ ID NO. 109), or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of 'Aph1a' encoded by a nucleic acid that hybridizes to the 'Aph1a' under low stringency conditions.

3. The protein complex according to No. 1 selected from complex (I) and comprising the following proteins:

- (i) "18 kDa microsomal signal peptidase subunit " (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "18 kDa microsomal signal peptidase subunit " encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit " nucleic acid or its complement under low stringency conditions,
- (ii) "23 kDa microsomal signal peptidase" (SEQ ID No:221) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "23 kDa microsomal signal peptidase" encoded by a nucleic acid that hybridizes to the "23 kDa microsomal signal peptidase" nucleic acid or its complement under low stringency conditions,
- (iii) "25 kDa microsomal signal peptidase subunit" (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "25 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "25 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,
- (iv) "ABCC1" (SEQ ID No:222) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ABCC1" encoded by a nucleic acid that hybridizes to the "ABCC1" nucleic acid or its complement under low stringency conditions,
- (v) "APLP2" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions,
- (vi) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
- (vii) "ATM" (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATM" encoded by a nucleic acid that hybridizes to the "ATM" nucleic acid or its complement under low stringency conditions,



(viii) "ATP-binding cassette, sub-family A member 3" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family A member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A member 3" nucleic acid or its complement under low stringency conditions,

(ix) "ATP1B1" (SEQ ID No:223) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP1B1" encoded by a nucleic acid that hybridizes to the "ATP1B1" nucleic acid or its complement under low stringency conditions,

(x) "ATP2C1" (SEQ ID No:224) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP2C1" encoded by a nucleic acid that hybridizes to the "ATP2C1" nucleic acid or its complement under low stringency conditions,

(xi) "Acetolactate synthase homolog" (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Acetolactate synthase homolog" encoded by a nucleic acid that hybridizes to the "Acetolactate synthase homolog" nucleic acid or its complement under low stringency conditions,

(xii) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,

(xiii) "Brain-specific GTP-binding protein" (SEQ ID No:225) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Brain-specific GTP-binding protein" encoded by a nucleic acid that hybridizes to the "Brain-specific GTP-binding protein" nucleic acid or its complement under low stringency conditions,

(xiv) "CDW92" (SEQ ID No:226) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDW92" encoded by a nucleic acid that hybridizes to the "CDW92" nucleic acid or its complement under low stringency conditions,

(xv) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a

nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,

(xvi) "CNTNAP1" (SEQ ID No:227) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CNTNAP1" encoded by a nucleic acid that hybridizes to the "CNTNAP1" nucleic acid or its complement under low stringency conditions,

(xvii) "Cerebral protein-10" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cerebral protein-10" encoded by a nucleic acid that hybridizes to the "Cerebral protein-10" nucleic acid or its complement under low stringency conditions,

(xviii) "DNM1" (SEQ ID No:228) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DNM1" encoded by a nucleic acid that hybridizes to the "DNM1" nucleic acid or its complement under low stringency conditions,

(xix) "Dihydrofolate reductase" (SEQ ID No:229) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dihydrofolate reductase" encoded by a nucleic acid that hybridizes to the "Dihydrofolate reductase" nucleic acid or its complement under low stringency conditions,

(xx) "ENG" (SEQ ID No:230) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENG" encoded by a nucleic acid that hybridizes to the "ENG" nucleic acid or its complement under low stringency conditions,

(xxi) "EXT2" (SEQ ID No:231) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EXT2" encoded by a nucleic acid that hybridizes to the "EXT2" nucleic acid or its complement under low stringency conditions,

(xxii) "EXTL3" (SEQ ID No:232) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EXTL3" encoded by a nucleic acid that hybridizes to the "EXTL3" nucleic acid or its complement under low stringency conditions,

(xxiii) "Endocytic receptor Endo180" (SEQ ID No:233) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Endocytic receptor Endo180" encoded by a nucleic acid that hybridizes to the

"Endocytic receptor Endo180" nucleic acid or its complement under low stringency conditions,

(xxiv) "FLJ13660" (SEQ ID No:234) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13660" encoded by a nucleic acid that hybridizes to the "FLJ13660" nucleic acid or its complement under low stringency conditions,

(xxv) "GPR49" (SEQ ID No:235) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GPR49" encoded by a nucleic acid that hybridizes to the "GPR49" nucleic acid or its complement under low stringency conditions,

(xxvi) "HK2" (SEQ ID No:236) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HK2" encoded by a nucleic acid that hybridizes to the "HK2" nucleic acid or its complement under low stringency conditions,

(xxvii) "HU-K4" (SEQ ID No:133) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HU-K4" encoded by a nucleic acid that hybridizes to the "HU-K4" nucleic acid or its complement under low stringency conditions,

(xxviii) "HUNC18a" (SEQ ID No:54) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HUNC18a" encoded by a nucleic acid that hybridizes to the "HUNC18a" nucleic acid or its complement under low stringency conditions,

(xxix) "HYPOTHETICAL PROTEIN " (SEQ ID No:237) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN " encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN " nucleic acid or its complement under low stringency conditions,

(xxx) "Hypothetical protein (Fragment)" (SEQ ID No:238) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein (Fragment)" encoded by a nucleic acid that hybridizes to the "Hypothetical protein (Fragment)" nucleic acid or its complement under low stringency conditions,

(xxxi) "Hypothetical protein FLJ14562" (SEQ ID No:239) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a

variant of "Hypothetical protein FLJ14562" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ14562" nucleic acid or its complement under low stringency conditions,

(xxxii) "Hypothetical protein FLJ23630" (SEQ ID No:240) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ23630" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ23630" nucleic acid or its complement under low stringency conditions,

(xxxiii) "Hypothetical protein KIAA0372" (SEQ ID No:241) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0372" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0372" nucleic acid or its complement under low stringency conditions,

(xxxiv) "ICAM2" (SEQ ID No:200) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ICAM2" encoded by a nucleic acid that hybridizes to the "ICAM2" nucleic acid or its complement under low stringency conditions,

(xxxv) "IGF2R" (SEQ ID No:242) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IGF2R" encoded by a nucleic acid that hybridizes to the "IGF2R" nucleic acid or its complement under low stringency conditions,

(xxxvi) "ITPR1" (SEQ ID No:243) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITPR1" encoded by a nucleic acid that hybridizes to the "ITPR1" nucleic acid or its complement under low stringency conditions,

(xxxvii) "Insulinoma-glucagonoma protein 20" (SEQ ID No:58) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Insulinoma-glucagonoma protein 20" encoded by a nucleic acid that hybridizes to the "Insulinoma-glucagonoma protein 20" nucleic acid or its complement under low stringency conditions,

(xxxviii) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that

hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions,

(xxxix) "KIAA0062 (FRAGMENT)" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0062 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0062 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xli) "KIAA0251 (FRAGMENT)" (SEQ ID No:244) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0251 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0251 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xlii) "KIAA0363 (FRAGMENT)" (SEQ ID No:245) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0363 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0363 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xliii) "KIAA0763" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions,

(xliv) "KIAA0971" (SEQ ID No:246) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0971" encoded by a nucleic acid that hybridizes to the "KIAA0971" nucleic acid or its complement under low stringency conditions,

(xlv) "KIAA1250" (SEQ ID No:247) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1250" encoded by a nucleic acid that hybridizes to the "KIAA1250" nucleic acid or its complement under low stringency conditions,

(xlv) "LRP5" (SEQ ID No:248) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LRP5" encoded by a nucleic acid that hybridizes to the "LRP5" nucleic acid or its complement under low stringency conditions,

(xlv) "MGC4248" (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4248" encoded by a nucleic acid that hybridizes to the "MGC4248" nucleic acid or its complement under low stringency conditions,

(xlvii) "Mesenchymal stem cell protein DSCD75" (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Mesenchymal stem cell protein DSCD75" encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75" nucleic acid or its complement under low stringency conditions,

(xlviii) "NRP2" (SEQ ID No:249) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NRP2" encoded by a nucleic acid that hybridizes to the "NRP2" nucleic acid or its complement under low stringency conditions,

(xlix) "Neurotrypsin" (SEQ ID No:206) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions,

(l) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,

(li) "PCDHA10" (SEQ ID No:250) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHA10" encoded by a nucleic acid that hybridizes to the "PCDHA10" nucleic acid or its complement under low stringency conditions,

(lii) "PCDHB12" (SEQ ID No:251) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB12" encoded by a nucleic acid that hybridizes to the "PCDHB12" nucleic acid or its complement under low stringency conditions,

(liii) "PCDHB13: protocadherin beta 13" (SEQ ID No:252) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB13: protocadherin beta 13" encoded by a nucleic acid that hybridizes to the "PCDHB13: protocadherin beta 13" nucleic acid or its complement under low stringency conditions,

(liv) "PCDHB4" (SEQ ID No:253) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB4" encoded by a nucleic acid that hybridizes to the "PCDHB4" nucleic acid or its complement under low stringency conditions,

- (lv) "PCDHGB1" (SEQ ID No:254) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHGB1" encoded by a nucleic acid that hybridizes to the "PCDHGB1" nucleic acid or its complement under low stringency conditions,
- (lvi) "PCDHGB6" (SEQ ID No:255) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHGB6" encoded by a nucleic acid that hybridizes to the "PCDHGB6" nucleic acid or its complement under low stringency conditions,
- (lvii) "PMPCB" (SEQ ID No:256) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PMPCB" encoded by a nucleic acid that hybridizes to the "PMPCB" nucleic acid or its complement under low stringency conditions,
- (lviii) "PP2C gamma" (SEQ ID No:257) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PP2C gamma" encoded by a nucleic acid that hybridizes to the "PP2C gamma" nucleic acid or its complement under low stringency conditions,
- (lix) "Pcdhb17" (SEQ ID No:258) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pcdhb17" encoded by a nucleic acid that hybridizes to the "Pcdhb17" nucleic acid or its complement under low stringency conditions,
- (lx) "Pen-2" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions,
- (lxi) "Presenilin 1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions,
- (lxii) "Presenilin 2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions,
- (lxiii) "Protocadherin 7" (SEQ ID No:259) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin

7" encoded by a nucleic acid that hybridizes to the "Protocadherin 7" nucleic acid or its complement under low stringency conditions,

(lxiv) "Protocadherin beta 16" (SEQ ID No:260) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"Protocadherin beta 16" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 16" nucleic acid or its complement under low stringency conditions,

(lxv) "Protocadherin beta 8" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"Protocadherin beta 8" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8" nucleic acid or its complement under low stringency conditions,

(lxvi) "RAB-18" (SEQ ID No:261) or a functionally active derivative thereof, or a

functionally active fragment thereof, or a homolog thereof, or a variant of "RAB-18" encoded by a nucleic acid that hybridizes to the "RAB-18" nucleic acid or its complement under low stringency conditions,

(lxvii) "RNASEL" (SEQ ID No:262) or a functionally active derivative thereof, or a

functionally active fragment thereof, or a homolog thereof, or a variant of "RNASEL" encoded by a nucleic acid that hybridizes to the "RNASEL" nucleic acid or its complement under low stringency conditions,

(lxviii) "Rab3 GTPase-activating protein, non-catalytic subunit" (SEQ ID No:263) or a

functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Rab3 GTPase-activating protein, non-catalytic subunit" encoded by a nucleic acid that hybridizes to the "Rab3 GTPase-activating protein, non-catalytic subunit" nucleic acid or its complement under low stringency conditions,

(lxix) "Retinal short-chain dehydrogenase/reductase retSDR2" (SEQ ID No:216) or a

functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2" encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2" nucleic acid or its complement under low stringency conditions,

(lxx) "SMAP-1B" (SEQ ID No:264) or a functionally active derivative thereof, or a

functionally active fragment thereof, or a homolog thereof, or a variant of "SMAP-1B" encoded by a nucleic acid that hybridizes to the "SMAP-1B" nucleic acid or its complement under low stringency conditions,



(lxxi) "SPTLC2" (SEQ ID No:265) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SPTLC2" encoded by a nucleic acid that hybridizes to the "SPTLC2" nucleic acid or its complement under low stringency conditions,

(lxxii) "STMN3" (SEQ ID No:87) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STMN3" encoded by a nucleic acid that hybridizes to the "STMN3" nucleic acid or its complement under low stringency conditions,

(lxxiii) "Sideroflexin 1" (SEQ ID No:266) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sideroflexin 1" encoded by a nucleic acid that hybridizes to the "Sideroflexin 1" nucleic acid or its complement under low stringency conditions,

(lxxiv) "Signal transducer and activator of transcription-1" (SEQ ID No:267) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Signal transducer and activator of transcription-1" encoded by a nucleic acid that hybridizes to the "Signal transducer and activator of transcription-1" nucleic acid or its complement under low stringency conditions,

(lxxv) "Similar to CGI-135 protein" (SEQ ID No:268) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to CGI-135 protein" encoded by a nucleic acid that hybridizes to the "Similar to CGI-135 protein" nucleic acid or its complement under low stringency conditions,

(lxxvi) "Sterile alpha and HEAT/Armadillo motif protein" (SEQ ID No:269) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sterile alpha and HEAT/Armadillo motif protein" encoded by a nucleic acid that hybridizes to the "Sterile alpha and HEAT/Armadillo motif protein" nucleic acid or its complement under low stringency conditions,

(lxxvii) "Sterol O-acyltransferase 1" (SEQ ID No:270) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sterol O-acyltransferase 1" encoded by a nucleic acid that hybridizes to the "Sterol O-acyltransferase 1" nucleic acid or its complement under low stringency conditions,

(lxxviii) "Thioredoxin domain-containing protein" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that

hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions,

(lxxix) "Triple functional domain protein (PTPRF interacting)" (SEQ ID No:271) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Triple functional domain protein (PTPRF interacting)" encoded by a nucleic acid that hybridizes to the "Triple functional domain protein (PTPRF interacting)" nucleic acid or its complement under low stringency conditions,

(lxxx) "UNC5C" (SEQ ID No:272) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "UNC5C" encoded by a nucleic acid that hybridizes to the "UNC5C" nucleic acid or its complement under low stringency conditions,

(lxxxi) "Vacuolar ATP synthase membrane sector associated protein m8-9" (SEQ ID No:273) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Vacuolar ATP synthase membrane sector associated protein m8-9" encoded by a nucleic acid that hybridizes to the "Vacuolar ATP synthase membrane sector associated protein m8-9" nucleic acid or its complement under low stringency conditions,

(lxxxii) "Y391\_HUMAN" (SEQ ID No:274) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Y391\_HUMAN" encoded by a nucleic acid that hybridizes to the "Y391\_HUMAN" nucleic acid or its complement under low stringency conditions,

(lxxxiii) "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" (SEQ ID No:275) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" nucleic acid or its complement under low stringency conditions,

(lxxxiv) "hypothetical protein MGC22916" (SEQ ID No:276) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC22916" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC22916" nucleic acid or its complement under low stringency conditions,

(lxxxv) "integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a

variant of "integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "integral membrane transporter protein" nucleic acid or its complement under low stringency conditions,

(lxxxvi) "tegt: testis enhanced gene transcript (bax inhibitor 1)" (SEQ ID No:278) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "tegt: testis enhanced gene transcript (bax inhibitor 1)" encoded by a nucleic acid that hybridizes to the "tegt: testis enhanced gene transcript (bax inhibitor 1)" nucleic acid or its complement under low stringency conditions, and/or (lxxxvii) "vacuolar protein sorting protein 18" (SEQ ID No:279) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "vacuolar protein sorting protein 18" encoded by a nucleic acid that hybridizes to the "vacuolar protein sorting protein 18" nucleic acid or its complement under low stringency conditions,

and a protein complex selected from complex (II) and comprising the following proteins:

(i) "18 kDa microsomal signal peptidase subunit " (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "18 kDa microsomal signal peptidase subunit " encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit " nucleic acid or its complement under low stringency conditions,

(ii) "23 kDa microsomal signal peptidase" (SEQ ID No:221) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "23 kDa microsomal signal peptidase" encoded by a nucleic acid that hybridizes to the "23 kDa microsomal signal peptidase" nucleic acid or its complement under low stringency conditions,

(iii) "25 kDa microsomal signal peptidase subunit" (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "25 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "25 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,

(iv) "ABCC1" (SEQ ID No:222) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ABCC1" encoded by a nucleic acid that hybridizes to the "ABCC1" nucleic acid or its complement under low stringency conditions,

- (v) "APLP2" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions,
- (vi) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
- (vii) "ATM" (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATM" encoded by a nucleic acid that hybridizes to the "ATM" nucleic acid or its complement under low stringency conditions,
- (viii) "ATP-binding cassette, sub-family A member 3" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family A member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A member 3" nucleic acid or its complement under low stringency conditions,
- (ix) "ATP1B1" (SEQ ID No:223) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP1B1" encoded by a nucleic acid that hybridizes to the "ATP1B1" nucleic acid or its complement under low stringency conditions,
- (x) "ATP2C1" (SEQ ID No:224) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP2C1" encoded by a nucleic acid that hybridizes to the "ATP2C1" nucleic acid or its complement under low stringency conditions,
- (xi) "Acetolactate synthase homolog" (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Acetolactate synthase homolog" encoded by a nucleic acid that hybridizes to the "Acetolactate synthase homolog" nucleic acid or its complement under low stringency conditions,
- (xii) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,

- (xiii) "Brain-specific GTP-binding protein" (SEQ ID No:225) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Brain-specific GTP-binding protein" encoded by a nucleic acid that hybridizes to the "Brain-specific GTP-binding protein" nucleic acid or its complement under low stringency conditions,
- (xiv) "CDW92" (SEQ ID No:226) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDW92" encoded by a nucleic acid that hybridizes to the "CDW92" nucleic acid or its complement under low stringency conditions,
- (xv) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,
- (xvi) "CNTNAP1" (SEQ ID No:227) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CNTNAP1" encoded by a nucleic acid that hybridizes to the "CNTNAP1" nucleic acid or its complement under low stringency conditions,
- (xvii) "Cerebral protein-10" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cerebral protein-10" encoded by a nucleic acid that hybridizes to the "Cerebral protein-10" nucleic acid or its complement under low stringency conditions,
- (xviii) "DNM1" (SEQ ID No:228) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DNM1" encoded by a nucleic acid that hybridizes to the "DNM1" nucleic acid or its complement under low stringency conditions,
- (xix) "Dihydrofolate reductase" (SEQ ID No:229) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dihydrofolate reductase" encoded by a nucleic acid that hybridizes to the "Dihydrofolate reductase" nucleic acid or its complement under low stringency conditions,
- (xx) "ENG" (SEQ ID No:230) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENG" encoded by a nucleic acid that hybridizes to the "ENG" nucleic acid or its complement under low stringency conditions,

- (xxi) "EXT2" (SEQ ID No:231) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EXT2" encoded by a nucleic acid that hybridizes to the "EXT2" nucleic acid or its complement under low stringency conditions,
- (xxii) "EXTL3" (SEQ ID No:232) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EXTL3" encoded by a nucleic acid that hybridizes to the "EXTL3" nucleic acid or its complement under low stringency conditions,
- (xxiii) "Endocytic receptor Endo180" (SEQ ID No:233) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Endocytic receptor Endo180" encoded by a nucleic acid that hybridizes to the "Endocytic receptor Endo180" nucleic acid or its complement under low stringency conditions,
- (xxiv) "FLJ13660" (SEQ ID No:234) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13660" encoded by a nucleic acid that hybridizes to the "FLJ13660" nucleic acid or its complement under low stringency conditions,
- (xxv) "GPR49" (SEQ ID No:235) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GPR49" encoded by a nucleic acid that hybridizes to the "GPR49" nucleic acid or its complement under low stringency conditions,
- (xxvi) "HK2" (SEQ ID No:236) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HK2" encoded by a nucleic acid that hybridizes to the "HK2" nucleic acid or its complement under low stringency conditions,
- (xxvii) "HU-K4" (SEQ ID No:133) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HU-K4" encoded by a nucleic acid that hybridizes to the "HU-K4" nucleic acid or its complement under low stringency conditions,
- (xxviii) "HUNC18a" (SEQ ID No:54) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HUNC18a" encoded by a nucleic acid that hybridizes to the "HUNC18a" nucleic acid or its complement under low stringency conditions,

(xxix) "HYPOTHETICAL PROTEIN " (SEQ ID No:237) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN " encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN " nucleic acid or its complement under low stringency conditions,

(xxx) "Hypothetical protein (Fragment)" (SEQ ID No:238) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein (Fragment)" encoded by a nucleic acid that hybridizes to the "Hypothetical protein (Fragment)" nucleic acid or its complement under low stringency conditions,

(xxxi) "Hypothetical protein FLJ14562" (SEQ ID No:239) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ14562" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ14562" nucleic acid or its complement under low stringency conditions,

(xxxii) "Hypothetical protein FLJ23630" (SEQ ID No:240) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ23630" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ23630" nucleic acid or its complement under low stringency conditions,

(xxxiii) "Hypothetical protein KIAA0372" (SEQ ID No:241) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0372" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0372" nucleic acid or its complement under low stringency conditions,

(xxxiv) "ICAM2" (SEQ ID No:200) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ICAM2" encoded by a nucleic acid that hybridizes to the "ICAM2" nucleic acid or its complement under low stringency conditions,

(xxxv) "IGF2R" (SEQ ID No:242) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IGF2R" encoded by a nucleic acid that hybridizes to the "IGF2R" nucleic acid or its complement under low stringency conditions,

(xxxvi) "ITPR1" (SEQ ID No:243) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITPR1" encoded by a nucleic acid that hybridizes to the "ITPR1" nucleic acid or its complement under low stringency conditions,

(xxxvii) "Insulinoma-glucagonoma protein 20" (SEQ ID No:58) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Insulinoma-glucagonoma protein 20" encoded by a nucleic acid that hybridizes to the "Insulinoma-glucagonoma protein 20" nucleic acid or its complement under low stringency conditions,

(xxxviii) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions,

(xxxix) "KIAA0062 (FRAGMENT)" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0062 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0062 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xl) "KIAA0251 (FRAGMENT)" (SEQ ID No:244) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0251 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0251 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xli) "KIAA0363 (FRAGMENT)" (SEQ ID No:245) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0363 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0363 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xlii) "KIAA0763" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions,

(xliii) "KIAA0971" (SEQ ID No:246) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0971" encoded by a nucleic acid that hybridizes to the "KIAA0971" nucleic acid or its complement under low stringency conditions,



(xliv) "KIAA1250" (SEQ ID No:247) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1250" encoded by a nucleic acid that hybridizes to the "KIAA1250" nucleic acid or its complement under low stringency conditions,

(xlv) "LRP5" (SEQ ID No:248) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LRP5" encoded by a nucleic acid that hybridizes to the "LRP5" nucleic acid or its complement under low stringency conditions,

(xlvii) "MGC4248 " (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4248 " encoded by a nucleic acid that hybridizes to the "MGC4248 " nucleic acid or its complement under low stringency conditions,

(xlviii) "Mesenchymal stem cell protein DSCD75" (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Mesenchymal stem cell protein DSCD75" encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75" nucleic acid or its complement under low stringency conditions,

(xlix) "NRP2" (SEQ ID No:249) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NRP2" encoded by a nucleic acid that hybridizes to the "NRP2" nucleic acid or its complement under low stringency conditions,

(l) "Neurotrypsin" (SEQ ID No:206) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions,

(ii) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,

(iii) "PCDHA10" (SEQ ID No:250) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHA10" encoded by a nucleic acid that hybridizes to the "PCDHA10" nucleic acid or its complement under low stringency conditions,

- (lii) "PCDHB12" (SEQ ID No:251) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB12" encoded by a nucleic acid that hybridizes to the "PCDHB12" nucleic acid or its complement under low stringency conditions,
- (liii) "PCDHB13: protocadherin beta 13" (SEQ ID No:252) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB13: protocadherin beta 13" encoded by a nucleic acid that hybridizes to the "PCDHB13: protocadherin beta 13" nucleic acid or its complement under low stringency conditions,
- (liv) "PCDHB4" (SEQ ID No:253) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB4" encoded by a nucleic acid that hybridizes to the "PCDHB4" nucleic acid or its complement under low stringency conditions,
- (lv) "PCDHGB1" (SEQ ID No:254) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHGB1" encoded by a nucleic acid that hybridizes to the "PCDHGB1" nucleic acid or its complement under low stringency conditions,
- (lvi) "PCDHGB6" (SEQ ID No:255) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHGB6" encoded by a nucleic acid that hybridizes to the "PCDHGB6" nucleic acid or its complement under low stringency conditions,
- (lvii) "PMPCB" (SEQ ID No:256) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PMPCB" encoded by a nucleic acid that hybridizes to the "PMPCB" nucleic acid or its complement under low stringency conditions,
- (lviii) "PP2C gamma" (SEQ ID No:257) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PP2C gamma" encoded by a nucleic acid that hybridizes to the "PP2C gamma" nucleic acid or its complement under low stringency conditions,
- (lix) "Pcdhb17" (SEQ ID No:258) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pcdhb17" encoded by a nucleic acid that hybridizes to the "Pcdhb17" nucleic acid or its complement under low stringency conditions,

- (Ix) "Presenilin 1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions,
- (Ixi) "Protocadherin 7" (SEQ ID No:259) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin 7" encoded by a nucleic acid that hybridizes to the "Protocadherin 7" nucleic acid or its complement under low stringency conditions,
- (Ixii) "Protocadherin beta 16" (SEQ ID No:260) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 16" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 16" nucleic acid or its complement under low stringency conditions,
- (Ixiii) "Protocadherin beta 8" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 8" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8" nucleic acid or its complement under low stringency conditions,
- (Ixiv) "RAB-18" (SEQ ID No:261) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB-18" encoded by a nucleic acid that hybridizes to the "RAB-18" nucleic acid or its complement under low stringency conditions,
- (Ixv) "RNASEL" (SEQ ID No:262) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RNASEL" encoded by a nucleic acid that hybridizes to the "RNASEL" nucleic acid or its complement under low stringency conditions,
- (Ixvi) "Rab3 GTPase-activating protein, non-catalytic subunit" (SEQ ID No:263) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Rab3 GTPase-activating protein, non-catalytic subunit" encoded by a nucleic acid that hybridizes to the "Rab3 GTPase-activating protein, non-catalytic subunit" nucleic acid or its complement under low stringency conditions,
- (Ixvii) "Retinal short-chain dehydrogenase/reductase retSDR2" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2" encoded by a nucleic acid that hybridizes to the "Retinal short-chain

dehydrogenase/reductase retSDR2" nucleic acid or its complement under low stringency conditions,

(Ixxviii) "SMAP-1B" (SEQ ID No:264) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SMAP-1B" encoded by a nucleic acid that hybridizes to the "SMAP-1B" nucleic acid or its complement under low stringency conditions,

(Ixxix) "SPTLC2" (SEQ ID No:265) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SPTLC2" encoded by a nucleic acid that hybridizes to the "SPTLC2" nucleic acid or its complement under low stringency conditions,

(Ixx) "STMN3" (SEQ ID No:87) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STMN3" encoded by a nucleic acid that hybridizes to the "STMN3" nucleic acid or its complement under low stringency conditions,

(Ixxxi) "Sideroflexin 1" (SEQ ID No:266) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sideroflexin 1" encoded by a nucleic acid that hybridizes to the "Sideroflexin 1" nucleic acid or its complement under low stringency conditions,

(Ixxii) "Signal transducer and activator of transcription-1" (SEQ ID No:267) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Signal transducer and activator of transcription-1" encoded by a nucleic acid that hybridizes to the "Signal transducer and activator of transcription-1" nucleic acid or its complement under low stringency conditions,

(Ixxiii) "Similar to CGI-135 protein" (SEQ ID No:268) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to CGI-135 protein" encoded by a nucleic acid that hybridizes to the "Similar to CGI-135 protein" nucleic acid or its complement under low stringency conditions,

(Ixxiv) "Sterile alpha and HEAT/Armadillo motif protein" (SEQ ID No:269) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sterile alpha and HEAT/Armadillo motif protein" encoded by a nucleic acid that hybridizes to the "Sterile alpha and HEAT/Armadillo motif protein" nucleic acid or its complement under low stringency conditions,

(Ixxv) "Sterol O-acyltransferase 1" (SEQ ID No:270) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"Sterol O-acyltransferase 1" encoded by a nucleic acid that hybridizes to the "Sterol O-acyltransferase 1" nucleic acid or its complement under low stringency conditions, (lxxvi) "Thioredoxin domain-containing protein" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions,

(lxxvii) "Triple functional domain protein (PTPRF interacting)" (SEQ ID No:271) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Triple functional domain protein (PTPRF interacting)" encoded by a nucleic acid that hybridizes to the "Triple functional domain protein (PTPRF interacting)" nucleic acid or its complement under low stringency conditions, (lxxviii) "UNC5C" (SEQ ID No:272) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "UNC5C" encoded by a nucleic acid that hybridizes to the "UNC5C" nucleic acid or its complement under low stringency conditions,

(lxxix) "Vacuolar ATP synthase membrane sector associated protein m8-9" (SEQ ID No:273) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Vacuolar ATP synthase membrane sector associated protein m8-9" encoded by a nucleic acid that hybridizes to the "Vacuolar ATP synthase membrane sector associated protein m8-9" nucleic acid or its complement under low stringency conditions,

(lxxx) "Y391\_HUMAN" (SEQ ID No:274) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Y391\_HUMAN" encoded by a nucleic acid that hybridizes to the "Y391\_HUMAN" nucleic acid or its complement under low stringency conditions,

(lxxxii) "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" (SEQ ID No:275) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" nucleic acid or its complement under low stringency conditions,

(lxxxii) "hypothetical protein MGC22916" (SEQ ID No:276) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a

variant of "hypothetical protein MGC22916" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC22916" nucleic acid or its complement under low stringency conditions,

(lxxxiii) "integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "integral membrane transporter protein" nucleic acid or its complement under low stringency conditions,

(lxxxiv) "tegt: testis enhanced gene transcript (bax inhibitor 1)" (SEQ ID No:278) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "tegt: testis enhanced gene transcript (bax inhibitor 1)" encoded by a nucleic acid that hybridizes to the "tegt: testis enhanced gene transcript (bax inhibitor 1)" nucleic acid or its complement under low stringency conditions, and/or (lxxxv) "vacuolar protein sorting protein 18" (SEQ ID No:279) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "vacuolar protein sorting protein 18" encoded by a nucleic acid that hybridizes to the "vacuolar protein sorting protein 18" nucleic acid or its complement under low stringency conditions.

4. The protein complex according to No. 1 comprising all but 1 - 81 of the following proteins:

(i) "18 kDa microsomal signal peptidase subunit " (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "18 kDa microsomal signal peptidase subunit " encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit " nucleic acid or its complement under low stringency conditions,

(ii) "23 kDa microsomal signal peptidase" (SEQ ID No:221) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "23 kDa microsomal signal peptidase" encoded by a nucleic acid that hybridizes to the "23 kDa microsomal signal peptidase" nucleic acid or its complement under low stringency conditions,

(iii) "25 kDa microsomal signal peptidase subunit" (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "25 kDa microsomal signal peptidase subunit" encoded by a nucleic acid

that hybridizes to the "25 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,

(iv) "ABCC1" (SEQ ID No:222) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ABCC1" encoded by a nucleic acid that hybridizes to the "ABCC1" nucleic acid or its complement under low stringency conditions,

(v) "APLP2" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions,

(vi) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,

(vii) "ATM" (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATM" encoded by a nucleic acid that hybridizes to the "ATM" nucleic acid or its complement under low stringency conditions,

(viii) "ATP-binding cassette, sub-family A member 3" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family A member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A member 3" nucleic acid or its complement under low stringency conditions,

(ix) "ATP1B1" (SEQ ID No:223) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP1B1" encoded by a nucleic acid that hybridizes to the "ATP1B1" nucleic acid or its complement under low stringency conditions,

(x) "ATP2C1" (SEQ ID No:224) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP2C1" encoded by a nucleic acid that hybridizes to the "ATP2C1" nucleic acid or its complement under low stringency conditions,

(xi) "Acetolactate synthase homolog" (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Acetolactate synthase homolog" encoded by a nucleic acid that hybridizes to the

"Acetolactate synthase homolog" nucleic acid or its complement under low stringency conditions,

(xii) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,

(xiii) "Brain-specific GTP-binding protein" (SEQ ID No:225) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Brain-specific GTP-binding protein" encoded by a nucleic acid that hybridizes to the "Brain-specific GTP-binding protein" nucleic acid or its complement under low stringency conditions,

(xiv) "CDW92" (SEQ ID No:226) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDW92" encoded by a nucleic acid that hybridizes to the "CDW92" nucleic acid or its complement under low stringency conditions,

(xv) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,

(xvi) "CNTNAP1" (SEQ ID No:227) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CNTNAP1" encoded by a nucleic acid that hybridizes to the "CNTNAP1" nucleic acid or its complement under low stringency conditions,

(xvii) "Cerebral protein-10" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cerebral protein-10" encoded by a nucleic acid that hybridizes to the "Cerebral protein-10" nucleic acid or its complement under low stringency conditions,

(xviii) "DNM1" (SEQ ID No:228) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DNM1" encoded by a nucleic acid that hybridizes to the "DNM1" nucleic acid or its complement under low stringency conditions,

(xix) "Dihydrofolate reductase" (SEQ ID No:229) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of



"Dihydrofolate reductase" encoded by a nucleic acid that hybridizes to the "Dihydrofolate reductase" nucleic acid or its complement under low stringency conditions,

(xx) "ENG" (SEQ ID No:230) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENG" encoded by a nucleic acid that hybridizes to the "ENG" nucleic acid or its complement under low stringency conditions,

(xxi) "EXT2" (SEQ ID No:231) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EXT2" encoded by a nucleic acid that hybridizes to the "EXT2" nucleic acid or its complement under low stringency conditions,

(xxii) "EXTL3" (SEQ ID No:232) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EXTL3" encoded by a nucleic acid that hybridizes to the "EXTL3" nucleic acid or its complement under low stringency conditions,

(xxiii) "Endocytic receptor Endo180" (SEQ ID No:233) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Endocytic receptor Endo180" encoded by a nucleic acid that hybridizes to the "Endocytic receptor Endo180" nucleic acid or its complement under low stringency conditions,

(xxiv) "FLJ13660" (SEQ ID No:234) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13660" encoded by a nucleic acid that hybridizes to the "FLJ13660" nucleic acid or its complement under low stringency conditions,

(xxv) "GPR49" (SEQ ID No:235) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GPR49" encoded by a nucleic acid that hybridizes to the "GPR49" nucleic acid or its complement under low stringency conditions,

(xxvi) "HK2" (SEQ ID No:236) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HK2" encoded by a nucleic acid that hybridizes to the "HK2" nucleic acid or its complement under low stringency conditions,

(xxvii) "HU-K4" (SEQ ID No:133) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HU-K4"

encoded by a nucleic acid that hybridizes to the "HU-K4" nucleic acid or its complement under low stringency conditions,

(xxviii) "HUNC18a" (SEQ ID No:54) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HUNC18a" encoded by a nucleic acid that hybridizes to the "HUNC18a" nucleic acid or its complement under low stringency conditions,

(xxix) "HYPOTHETICAL PROTEIN " (SEQ ID No:237) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN " encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN " nucleic acid or its complement under low stringency conditions,

(xxx) "Hypothetical protein (Fragment)" (SEQ ID No:238) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein (Fragment)" encoded by a nucleic acid that hybridizes to the "Hypothetical protein (Fragment)" nucleic acid or its complement under low stringency conditions,

(xxxi) "Hypothetical protein FLJ14562" (SEQ ID No:239) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ14562" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ14562" nucleic acid or its complement under low stringency conditions,

(xxxii) "Hypothetical protein FLJ23630" (SEQ ID No:240) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ23630" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ23630" nucleic acid or its complement under low stringency conditions,

(xxxiii) "Hypothetical protein KIAA0372" (SEQ ID No:241) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0372" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0372" nucleic acid or its complement under low stringency conditions,

(xxxiv) "ICAM2" (SEQ ID No:200) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ICAM2"

encoded by a nucleic acid that hybridizes to the "ICAM2" nucleic acid or its complement under low stringency conditions,

(xxxv) "IGF2R" (SEQ ID No:242) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IGF2R" encoded by a nucleic acid that hybridizes to the "IGF2R" nucleic acid or its complement under low stringency conditions,

(xxxvi) "ITPR1" (SEQ ID No:243) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITPR1" encoded by a nucleic acid that hybridizes to the "ITPR1" nucleic acid or its complement under low stringency conditions,

(xxxvii) "Insulinoma-glucagonoma protein 20" (SEQ ID No:58) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Insulinoma-glucagonoma protein 20" encoded by a nucleic acid that hybridizes to the "Insulinoma-glucagonoma protein 20" nucleic acid or its complement under low stringency conditions,

(xxxviii) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions,

(xxxix) "KIAA0062 (FRAGMENT)" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0062 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0062 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xl) "KIAA0251 (FRAGMENT)" (SEQ ID No:244) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0251 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0251 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xli) "KIAA0363 (FRAGMENT)" (SEQ ID No:245) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0363 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0363 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xlii) "KIAA0763" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0763"

encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions,

(xliii) "KIAA0971" (SEQ ID No:246) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0971" encoded by a nucleic acid that hybridizes to the "KIAA0971" nucleic acid or its complement under low stringency conditions,

(xliv) "KIAA1250" (SEQ ID No:247) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1250" encoded by a nucleic acid that hybridizes to the "KIAA1250" nucleic acid or its complement under low stringency conditions,

(xlv) "LRP5" (SEQ ID No:248) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LRP5" encoded by a nucleic acid that hybridizes to the "LRP5" nucleic acid or its complement under low stringency conditions,

(xlvi) "MGC4248 " (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4248 " encoded by a nucleic acid that hybridizes to the "MGC4248 " nucleic acid or its complement under low stringency conditions,

(xlvii) "Mesenchymal stem cell protein DSCD75" (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Mesenchymal stem cell protein DSCD75" encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75" nucleic acid or its complement under low stringency conditions,

(xlviii) "NRP2" (SEQ ID No:249) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NRP2" encoded by a nucleic acid that hybridizes to the "NRP2" nucleic acid or its complement under low stringency conditions,

(xlix) "Neurotrypsin" (SEQ ID No:206) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions,

(l) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a

nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,

(li) "PCDHA10" (SEQ ID No:250) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHA10" encoded by a nucleic acid that hybridizes to the "PCDHA10" nucleic acid or its complement under low stringency conditions,

(lii) "PCDHB12" (SEQ ID No:251) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB12" encoded by a nucleic acid that hybridizes to the "PCDHB12" nucleic acid or its complement under low stringency conditions,

(liii) "PCDHB13: protocadherin beta 13" (SEQ ID No:252) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB13: protocadherin beta 13" encoded by a nucleic acid that hybridizes to the "PCDHB13: protocadherin beta 13" nucleic acid or its complement under low stringency conditions,

(liv) "PCDHB4" (SEQ ID No:253) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB4" encoded by a nucleic acid that hybridizes to the "PCDHB4" nucleic acid or its complement under low stringency conditions,

(lv) "PCDHGB1" (SEQ ID No:254) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHGB1" encoded by a nucleic acid that hybridizes to the "PCDHGB1" nucleic acid or its complement under low stringency conditions,

(lvi) "PCDHGB6" (SEQ ID No:255) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHGB6" encoded by a nucleic acid that hybridizes to the "PCDHGB6" nucleic acid or its complement under low stringency conditions,

(lvii) "PMPCB" (SEQ ID No:256) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PMPCB" encoded by a nucleic acid that hybridizes to the "PMPCB" nucleic acid or its complement under low stringency conditions,

(lviii) "PP2C gamma" (SEQ ID No:257) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PP2C gamma"

encoded by a nucleic acid that hybridizes to the "PP2C gamma" nucleic acid or its complement under low stringency conditions,

(lix) "Pcdhb17" (SEQ ID No:258) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pcdhb17" encoded by a nucleic acid that hybridizes to the "Pcdhb17" nucleic acid or its complement under low stringency conditions,

(lx) "Pen-2" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions,

(lxi) "Presenilin 1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions,

(lxii) "Presenilin 2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions,

(lxiii) "Protocadherin 7" (SEQ ID No:259) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin 7" encoded by a nucleic acid that hybridizes to the "Protocadherin 7" nucleic acid or its complement under low stringency conditions,

(lxiv) "Protocadherin beta 16" (SEQ ID No:260) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 16" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 16" nucleic acid or its complement under low stringency conditions,

(lxv) "Protocadherin beta 8" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 8" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8" nucleic acid or its complement under low stringency conditions,

(lxvi) "RAB-18" (SEQ ID No:261) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB-18" encoded by a nucleic acid that hybridizes to the "RAB-18" nucleic acid or its complement under low stringency conditions,

(Ixxvii) "RNASEL" (SEQ ID No:262) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RNASEL" encoded by a nucleic acid that hybridizes to the "RNASEL" nucleic acid or its complement under low stringency conditions,

(Ixxviii) "Rab3 GTPase-activating protein, non-catalytic subunit" (SEQ ID No:263) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Rab3 GTPase-activating protein, non-catalytic subunit" encoded by a nucleic acid that hybridizes to the "Rab3 GTPase-activating protein, non-catalytic subunit" nucleic acid or its complement under low stringency conditions,

(Ixxix) "Retinal short-chain dehydrogenase/reductase retSDR2" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2" encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2" nucleic acid or its complement under low stringency conditions,

(Ixx) "SMAP-1B" (SEQ ID No:264) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SMAP-1B" encoded by a nucleic acid that hybridizes to the "SMAP-1B" nucleic acid or its complement under low stringency conditions,

(Ixxxi) "SPTLC2" (SEQ ID No:265) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SPTLC2" encoded by a nucleic acid that hybridizes to the "SPTLC2" nucleic acid or its complement under low stringency conditions,

(Ixxii) "STMN3" (SEQ ID No:87) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STMN3" encoded by a nucleic acid that hybridizes to the "STMN3" nucleic acid or its complement under low stringency conditions,

(Ixxiii) "Sideroflexin 1" (SEQ ID No:266) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sideroflexin 1" encoded by a nucleic acid that hybridizes to the "Sideroflexin 1" nucleic acid or its complement under low stringency conditions,

(Ixxiv) "Signal transducer and activator of transcription-1" (SEQ ID No:267) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Signal transducer and activator of transcription-1"

encoded by a nucleic acid that hybridizes to the "Signal transducer and activator of transcription-1" nucleic acid or its complement under low stringency conditions,

(lxxv) "Similar to CGI-135 protein" (SEQ ID No:268) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to CGI-135 protein" encoded by a nucleic acid that hybridizes to the "Similar to CGI-135 protein" nucleic acid or its complement under low stringency conditions,

(lxxvi) "Sterile alpha and HEAT/Armadillo motif protein" (SEQ ID No:269) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sterile alpha and HEAT/Armadillo motif protein" encoded by a nucleic acid that hybridizes to the "Sterile alpha and HEAT/Armadillo motif protein" nucleic acid or its complement under low stringency conditions,

(lxxvii) "Sterol O-acyltransferase 1" (SEQ ID No:270) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sterol O-acyltransferase 1" encoded by a nucleic acid that hybridizes to the "Sterol O-acyltransferase 1" nucleic acid or its complement under low stringency conditions,

(lxxviii) "Thioredoxin domain-containing protein" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions,

(lxxix) "Triple functional domain protein (PTPRF interacting)" (SEQ ID No:271) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Triple functional domain protein (PTPRF interacting)" encoded by a nucleic acid that hybridizes to the "Triple functional domain protein (PTPRF interacting)" nucleic acid or its complement under low stringency conditions,

(lxxx) "UNC5C" (SEQ ID No:272) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "UNC5C" encoded by a nucleic acid that hybridizes to the "UNC5C" nucleic acid or its complement under low stringency conditions,

(lxxxi) "Vacuolar ATP synthase membrane sector associated protein m8-9" (SEQ ID No:273) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Vacuolar ATP synthase membrane sector associated protein m8-9" encoded by a nucleic acid that hybridizes to the "Vacuolar ATP



synthase membrane sector associated protein m8-9" nucleic acid or its complement under low stringency conditions,

(lxxxii) "Y391\_HUMAN" (SEQ ID No:274) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Y391\_HUMAN" encoded by a nucleic acid that hybridizes to the "Y391\_HUMAN" nucleic acid or its complement under low stringency conditions,

(lxxxiii) "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" (SEQ ID No:275) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" nucleic acid or its complement under low stringency conditions,

(lxxxiv) "hypothetical protein MGC22916" (SEQ ID No:276) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC22916" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC22916" nucleic acid or its complement under low stringency conditions,

(lxxxv) "integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "integral membrane transporter protein" nucleic acid or its complement under low stringency conditions,

(lxxxvi) "tegt: testis enhanced gene transcript (bax inhibitor 1)" (SEQ ID No:278) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "tegt: testis enhanced gene transcript (bax inhibitor 1)" encoded by a nucleic acid that hybridizes to the "tegt: testis enhanced gene transcript (bax inhibitor 1)" nucleic acid or its complement under low stringency conditions,

(lxxxvii) "vacuolar protein sorting protein 18" (SEQ ID No:279) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "vacuolar protein sorting protein 18" encoded by a nucleic acid that hybridizes to the "vacuolar protein sorting protein 18" nucleic acid or its complement under low stringency conditions.

5. The complex of any of No. 1 - 4 comprising a functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein, respectively.

6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.

7. The complex of any of No. 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.

8. The complex of any of No. 1 - 7 that is involved in the the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)).

9. A process for preparing a complex of any of No. 1 - 8 and optionally the components thereof comprising the following steps: expressing a protein (bait) of the complex, preferably a tagged protein, in a target cell, isolating the protein complex which is attached to the bait protein, and optionally dissociating the protein complex and isolating the individual complex members.

10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.
11. The process according to any of No. 9 - 10 wherein the two tags are separated by a cleavage site for a protease.
12. Component of the Aph-1a complex obtainable by a process according to any of No. 9 - 11.
13. Protein of the Aph-1a complex selected from
- (i) "ABCC1" (SEQ ID No:222) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ABCC1" encoded by a nucleic acid that hybridizes to the "ABCC1" nucleic acid or its complement under low stringency conditions,
  - (ii) "ATP-binding cassette, sub-family A member 3" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family A member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A member 3" nucleic acid or its complement under low stringency conditions,
  - (iii) "Acetolactate synthase homolog" (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Acetolactate synthase homolog" encoded by a nucleic acid that hybridizes to the "Acetolactate synthase homolog" nucleic acid or its complement under low stringency conditions,
  - (iv) "CDW92" (SEQ ID No:226) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDW92" encoded by a nucleic acid that hybridizes to the "CDW92" nucleic acid or its complement under low stringency conditions,
  - (v) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,
  - (vi) "Cerebral protein-10" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cerebral

protein-10" encoded by a nucleic acid that hybridizes to the "Cerebral protein-10" nucleic acid or its complement under low stringency conditions,

(vii) "GPR49" (SEQ ID No:235) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GPR49" encoded by a nucleic acid that hybridizes to the "GPR49" nucleic acid or its complement under low stringency conditions,

(viii) "HYPOTHETICAL PROTEIN " (SEQ ID No:237) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN " encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN " nucleic acid or its complement under low stringency conditions,

(ix) "Hypothetical protein (Fragment)" (SEQ ID No:238) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein (Fragment)" encoded by a nucleic acid that hybridizes to the "Hypothetical protein (Fragment)" nucleic acid or its complement under low stringency conditions,

(x) "Hypothetical protein FLJ14562" (SEQ ID No:239) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ14562" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ14562" nucleic acid or its complement under low stringency conditions,

(xi) "Hypothetical protein FLJ23630" (SEQ ID No:240) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ23630" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ23630" nucleic acid or its complement under low stringency conditions,

(xii) "Hypothetical protein KIAA0372" (SEQ ID No:241) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0372" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0372" nucleic acid or its complement under low stringency conditions,

(xiii) "KIAA0062 (FRAGMENT)" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"KIAA0062 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0062 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xiv) "KIAA0251 (FRAGMENT)" (SEQ ID No:244) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0251 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0251 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xv) "KIAA0363 (FRAGMENT)" (SEQ ID No:245) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0363 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0363 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xvi) "KIAA0763" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions,

(xvii) "KIAA0971" (SEQ ID No:246) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0971" encoded by a nucleic acid that hybridizes to the "KIAA0971" nucleic acid or its complement under low stringency conditions,

(xviii) "KIAA1250" (SEQ ID No:247) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1250" encoded by a nucleic acid that hybridizes to the "KIAA1250" nucleic acid or its complement under low stringency conditions,

(xix) "MGC4248 " (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4248 " encoded by a nucleic acid that hybridizes to the "MGC4248 " nucleic acid or its complement under low stringency conditions,

(xx) "Mesenchymal stem cell protein DSCD75" (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Mesenchymal stem cell protein DSCD75" encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75" nucleic acid or its complement under low stringency conditions,

(xxi) "PCDHA10" (SEQ ID No:250) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHA10"

encoded by a nucleic acid that hybridizes to the "PCDHA10" nucleic acid or its complement under low stringency conditions,

(xxii) "PCDHB12" (SEQ ID No:251) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB12" encoded by a nucleic acid that hybridizes to the "PCDHB12" nucleic acid or its complement under low stringency conditions,

(xxiii) "PCDHB13: protocadherin beta 13" (SEQ ID No:252) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB13: protocadherin beta 13" encoded by a nucleic acid that hybridizes to the "PCDHB13: protocadherin beta 13" nucleic acid or its complement under low stringency conditions,

(xxiv) "PCDHB4" (SEQ ID No:253) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB4" encoded by a nucleic acid that hybridizes to the "PCDHB4" nucleic acid or its complement under low stringency conditions,

(xxv) "PCDHGB1" (SEQ ID No:254) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHGB1" encoded by a nucleic acid that hybridizes to the "PCDHGB1" nucleic acid or its complement under low stringency conditions,

(xxvi) "PCDHGB6" (SEQ ID No:255) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHGB6" encoded by a nucleic acid that hybridizes to the "PCDHGB6" nucleic acid or its complement under low stringency conditions,

(xxvii) "Pcdhb17" (SEQ ID No:258) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pcdhb17" encoded by a nucleic acid that hybridizes to the "Pcdhb17" nucleic acid or its complement under low stringency conditions,

(xxviii) "Protocadherin 7" (SEQ ID No:259) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin 7" encoded by a nucleic acid that hybridizes to the "Protocadherin 7" nucleic acid or its complement under low stringency conditions,

(xxix) "Protocadherin beta 16" (SEQ ID No:260) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"Protocadherin beta 16" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 16" nucleic acid or its complement under low stringency conditions,

(xxx) "Protocadherin beta 8" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"Protocadherin beta 8" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8" nucleic acid or its complement under low stringency conditions,

(xxxi) "Retinal short-chain dehydrogenase/reductase retSDR2" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2" encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2" nucleic acid or its complement under low stringency conditions,

(xxxii) "Similar to CGI-135 protein" (SEQ ID No:268) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to CGI-135 protein" encoded by a nucleic acid that hybridizes to the "Similar to CGI-135 protein" nucleic acid or its complement under low stringency conditions,

(xxxiii) "Sterile alpha and HEAT/Armadillo motif protein" (SEQ ID No:269) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sterile alpha and HEAT/Armadillo motif protein" encoded by a nucleic acid that hybridizes to the "Sterile alpha and HEAT/Armadillo motif protein" nucleic acid or its complement under low stringency conditions,

(xxxiv) "Thioredoxin domain-containing protein" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions,

(xxxv) "Vacuolar ATP synthase membrane sector associated protein m8-9" (SEQ ID No:273) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Vacuolar ATP synthase membrane sector associated protein m8-9" encoded by a nucleic acid that hybridizes to the "Vacuolar ATP synthase membrane sector associated protein m8-9" nucleic acid or its complement under low stringency conditions,

(xxxvi) "Y391\_HUMAN" (SEQ ID No:274) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"Y391\_HUMAN" encoded by a nucleic acid that hybridizes to the "Y391\_HUMAN" nucleic acid or its complement under low stringency conditions,

(xxxvii) "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" (SEQ ID No:275) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" nucleic acid or its complement under low stringency conditions,

(xxxviii) "hypothetical protein MGC22916" (SEQ ID No:276) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC22916" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC22916" nucleic acid or its complement under low stringency conditions,

(xxxix) "integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "integral membrane transporter protein" nucleic acid or its complement under low stringency conditions, and

(xl) "tegt: testis enhanced gene transcript (bax inhibitor 1)" (SEQ ID No:278) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "tegt: testis enhanced gene transcript (bax inhibitor 1)" encoded by a nucleic acid that hybridizes to the "tegt: testis enhanced gene transcript (bax inhibitor 1)" nucleic acid or its complement under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

14. Nucleic acid encoding a protein according to No. 13.



15. Construct, preferably a vector construct, comprising (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or

(b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative of at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the second group of proteins according to No. 1 (b).

16. Host cell, containing a vector comprising at least one of the nucleic acid of No. 14 and/or a construct of No. 15 or containing several vectors each comprising at least the nucleic acid sequence encoding at least one of the proteins, or functionally active fragments or functionally active derivatives thereof selected from the first group of proteins according to No. 1 (a) and the proteins, or functionally active fragments or functionally active derivatives thereof selected from the second group of proteins according to No. 1 (b).

17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody which binds to any of the proteins according to No. 13.

18. A kit comprising in one or more container the complex of any of No. 1 - 8 and/or the proteins of No. 13 optionally together with an antibody according to No. 17 and/or further components such as reagents and working instructions.

19. The kit according to No. 18 for processing a substrate of said complex.

20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

21. Array, in which at least a complex according to any of No. 1 - 8 and/or at least one protein according to No. 14 and/or at least one antibody according to No. 17 is attached to a solid carrier.

22. A process for processing a physiological substrate of the complex comprising the step of bringing into contact a complex to any of No. 1 - 8 with said substrate, such that said substrate is processed.

23. A pharmaceutical composition comprising the protein complex of any of No. 1 - 8 and/or any of the following the proteins:

- (i) "ABCC1" (SEQ ID No:222) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ABCC1" encoded by a nucleic acid that hybridizes to the "ABCC1" nucleic acid or its complement under low stringency conditions,
- (ii) "ATP-binding cassette, sub-family A member 3" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family A member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A member 3" nucleic acid or its complement under low stringency conditions,
- (iii) "Acetolactate synthase homolog" (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Acetolactate synthase homolog" encoded by a nucleic acid that hybridizes to the "Acetolactate synthase homolog" nucleic acid or its complement under low stringency conditions,
- (iv) "CDW92" (SEQ ID No:226) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDW92" encoded by a nucleic acid that hybridizes to the "CDW92" nucleic acid or its complement under low stringency conditions,
- (v) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,

- (vi) "Cerebral protein-10" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cerebral protein-10" encoded by a nucleic acid that hybridizes to the "Cerebral protein-10" nucleic acid or its complement under low stringency conditions,
- (vii) "GPR49" (SEQ ID No:235) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GPR49" encoded by a nucleic acid that hybridizes to the "GPR49" nucleic acid or its complement under low stringency conditions,
- (viii) "HYPOTHETICAL PROTEIN " (SEQ ID No:237) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN " encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN " nucleic acid or its complement under low stringency conditions,
- (ix) "Hypothetical protein (Fragment)" (SEQ ID No:238) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein (Fragment)" encoded by a nucleic acid that hybridizes to the "Hypothetical protein (Fragment)" nucleic acid or its complement under low stringency conditions,
- (x) "Hypothetical protein FLJ14562" (SEQ ID No:239) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ14562" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ14562" nucleic acid or its complement under low stringency conditions,
- (xi) "Hypothetical protein FLJ23630" (SEQ ID No:240) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ23630" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ23630" nucleic acid or its complement under low stringency conditions,
- (xii) "Hypothetical protein KIAA0372" (SEQ ID No:241) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0372" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0372" nucleic acid or its complement under low stringency conditions,

- (xiii) "KIAA0062 (FRAGMENT)" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0062 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0062 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (xiv) "KIAA0251 (FRAGMENT)" (SEQ ID No:244) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0251 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0251 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (xv) "KIAA0363 (FRAGMENT)" (SEQ ID No:245) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0363 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0363 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (xvi) "KIAA0763" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions,
- (xvii) "KIAA0971" (SEQ ID No:246) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0971" encoded by a nucleic acid that hybridizes to the "KIAA0971" nucleic acid or its complement under low stringency conditions,
- (xviii) "KIAA1250" (SEQ ID No:247) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1250" encoded by a nucleic acid that hybridizes to the "KIAA1250" nucleic acid or its complement under low stringency conditions,
- (xix) "MGC4248 " (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4248 " encoded by a nucleic acid that hybridizes to the "MGC4248 " nucleic acid or its complement under low stringency conditions,
- (xx) "Mesenchymal stem cell protein DSCD75" (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Mesenchymal stem cell protein DSCD75" encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75" nucleic acid or its complement under low stringency conditions,

- (xxi) "PCDHA10" (SEQ ID No:250) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHA10" encoded by a nucleic acid that hybridizes to the "PCDHA10" nucleic acid or its complement under low stringency conditions,
- (xxii) "PCDHB12" (SEQ ID No:251) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB12" encoded by a nucleic acid that hybridizes to the "PCDHB12" nucleic acid or its complement under low stringency conditions,
- (xxiii) "PCDHB13: protocadherin beta 13" (SEQ ID No:252) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB13: protocadherin beta 13" encoded by a nucleic acid that hybridizes to the "PCDHB13: protocadherin beta 13" nucleic acid or its complement under low stringency conditions,
- (xxiv) "PCDHB4" (SEQ ID No:253) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB4" encoded by a nucleic acid that hybridizes to the "PCDHB4" nucleic acid or its complement under low stringency conditions,
- (xxv) "PCDHGB1" (SEQ ID No:254) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHGB1" encoded by a nucleic acid that hybridizes to the "PCDHGB1" nucleic acid or its complement under low stringency conditions,
- (xxvi) "PCDHGB6" (SEQ ID No:255) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHGB6" encoded by a nucleic acid that hybridizes to the "PCDHGB6" nucleic acid or its complement under low stringency conditions,
- (xxvii) "Pcdhb17" (SEQ ID No:258) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pcdhb17" encoded by a nucleic acid that hybridizes to the "Pcdhb17" nucleic acid or its complement under low stringency conditions,
- (xxviii) "Protocadherin 7" (SEQ ID No:259) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin 7" encoded by a nucleic acid that hybridizes to the "Protocadherin 7" nucleic acid or its complement under low stringency conditions,

- (xxix) "Protocadherin beta 16" (SEQ ID No:260) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 16" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 16" nucleic acid or its complement under low stringency conditions,
- (xxx) "Protocadherin beta 8" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 8" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8" nucleic acid or its complement under low stringency conditions,
- (xxxi) "Retinal short-chain dehydrogenase/reductase retSDR2" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2" encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2" nucleic acid or its complement under low stringency conditions,
- (xxxii) "Similar to CGI-135 protein" (SEQ ID No:268) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to CGI-135 protein" encoded by a nucleic acid that hybridizes to the "Similar to CGI-135 protein" nucleic acid or its complement under low stringency conditions,
- (xxxiii) "Sterile alpha and HEAT/Armadillo motif protein" (SEQ ID No:269) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sterile alpha and HEAT/Armadillo motif protein" encoded by a nucleic acid that hybridizes to the "Sterile alpha and HEAT/Armadillo motif protein" nucleic acid or its complement under low stringency conditions,
- (xxxiv) "Thioredoxin domain-containing protein" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions,
- (xxxv) "Vacuolar ATP synthase membrane sector associated protein m8-9" (SEQ ID No:273) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Vacuolar ATP synthase membrane sector associated protein m8-9" encoded by a nucleic acid that hybridizes to the "Vacuolar ATP synthase membrane sector associated protein m8-9" nucleic acid or its complement under low stringency conditions,

(xxxvi) "Y391\_HUMAN" (SEQ ID No:274) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Y391\_HUMAN" encoded by a nucleic acid that hybridizes to the "Y391\_HUMAN" nucleic acid or its complement under low stringency conditions,

(xxxvii) "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" (SEQ ID No:275) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" nucleic acid or its complement under low stringency conditions,

(xxxviii) "hypothetical protein MGC22916" (SEQ ID No:276) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC22916" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC22916" nucleic acid or its complement under low stringency conditions,

(xxxix) "integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "integral membrane transporter protein" nucleic acid or its complement under low stringency conditions, and/or

(xl) "tegt: testis enhanced gene transcript (bax inhibitor 1)" (SEQ ID No:278) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "tegt: testis enhanced gene transcript (bax inhibitor 1)" encoded by a nucleic acid that hybridizes to the "tegt: testis enhanced gene transcript (bax inhibitor 1)" nucleic acid or its complement under low stringency conditions, and a pharmaceutical acceptable carrier.

24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

25. A method for screening for a molecule that binds to the complex of anyone of No. 1 - 8 and/or any of the following the proteins:

- (i) "ABCC1" (SEQ ID No:222) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ABCC1" encoded by a nucleic acid that hybridizes to the "ABCC1" nucleic acid or its complement under low stringency conditions,
- (ii) "ATP-binding cassette, sub-family A member 3" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family A member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A member 3" nucleic acid or its complement under low stringency conditions,
- (iii) "Acetolactate synthase homolog" (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Acetolactate synthase homolog" encoded by a nucleic acid that hybridizes to the "Acetolactate synthase homolog" nucleic acid or its complement under low stringency conditions,
- (iv) "CDW92" (SEQ ID No:226) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDW92" encoded by a nucleic acid that hybridizes to the "CDW92" nucleic acid or its complement under low stringency conditions,
- (v) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,
- (vi) "Cerebral protein-10" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cerebral protein-10" encoded by a nucleic acid that hybridizes to the "Cerebral protein-10" nucleic acid or its complement under low stringency conditions,
- (vii) "GPR49" (SEQ ID No:235) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GPR49" encoded by a nucleic acid that hybridizes to the "GPR49" nucleic acid or its complement under low stringency conditions,
- (viii) "HYPOTHETICAL PROTEIN " (SEQ ID No:237) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN " encoded by a nucleic acid that hybridizes to the



"HYPOTHETICAL PROTEIN " nucleic acid or its complement under low stringency conditions,

(ix) "Hypothetical protein (Fragment)" (SEQ ID No:238) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein (Fragment)" encoded by a nucleic acid that hybridizes to the "Hypothetical protein (Fragment)" nucleic acid or its complement under low stringency conditions,

(x) "Hypothetical protein FLJ14562" (SEQ ID No:239) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ14562" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ14562" nucleic acid or its complement under low stringency conditions,

(xi) "Hypothetical protein FLJ23630" (SEQ ID No:240) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ23630" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ23630" nucleic acid or its complement under low stringency conditions,

(xii) "Hypothetical protein KIAA0372" (SEQ ID No:241) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0372" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0372" nucleic acid or its complement under low stringency conditions,

(xiii) "KIAA0062 (FRAGMENT)" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0062 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0062 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xiv) "KIAA0251 (FRAGMENT)" (SEQ ID No:244) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0251 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0251 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xv) "KIAA0363 (FRAGMENT)" (SEQ ID No:245) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0363 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0363 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

- (xvi) "KIAA0763" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions,
- (xvii) "KIAA0971" (SEQ ID No:246) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0971" encoded by a nucleic acid that hybridizes to the "KIAA0971" nucleic acid or its complement under low stringency conditions,
- (xviii) "KIAA1250" (SEQ ID No:247) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1250" encoded by a nucleic acid that hybridizes to the "KIAA1250" nucleic acid or its complement under low stringency conditions,
- (xix) "MGC4248 " (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4248 " encoded by a nucleic acid that hybridizes to the "MGC4248 " nucleic acid or its complement under low stringency conditions,
- (xx) "Mesenchymal stem cell protein DSCD75" (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Mesenchymal stem cell protein DSCD75" encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75" nucleic acid or its complement under low stringency conditions,
- (xxi) "PCDHA10" (SEQ ID No:250) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHA10" encoded by a nucleic acid that hybridizes to the "PCDHA10" nucleic acid or its complement under low stringency conditions,
- (xxii) "PCDHB12" (SEQ ID No:251) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB12" encoded by a nucleic acid that hybridizes to the "PCDHB12" nucleic acid or its complement under low stringency conditions,
- (xxiii) "PCDHB13: protocadherin beta 13" (SEQ ID No:252) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB13: protocadherin beta 13" encoded by a nucleic acid that hybridizes to the "PCDHB13: protocadherin beta 13" nucleic acid or its complement under low stringency conditions,

- (xxiv) "PCDHB4" (SEQ ID No:253) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB4" encoded by a nucleic acid that hybridizes to the "PCDHB4" nucleic acid or its complement under low stringency conditions,
- (xxv) "PCDHGB1" (SEQ ID No:254) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHGB1" encoded by a nucleic acid that hybridizes to the "PCDHGB1" nucleic acid or its complement under low stringency conditions,
- (xxvi) "PCDHGB6" (SEQ ID No:255) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHGB6" encoded by a nucleic acid that hybridizes to the "PCDHGB6" nucleic acid or its complement under low stringency conditions,
- (xxvii) "Pcdhb17" (SEQ ID No:258) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pcdhb17" encoded by a nucleic acid that hybridizes to the "Pcdhb17" nucleic acid or its complement under low stringency conditions,
- (xxviii) "Protocadherin 7" (SEQ ID No:259) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin 7" encoded by a nucleic acid that hybridizes to the "Protocadherin 7" nucleic acid or its complement under low stringency conditions,
- (xxix) "Protocadherin beta 16" (SEQ ID No:260) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 16" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 16" nucleic acid or its complement under low stringency conditions,
- (xxx) "Protocadherin beta 8" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 8" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8" nucleic acid or its complement under low stringency conditions,
- (xxxi) "Retinal short-chain dehydrogenase/reductase retSDR2" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2" encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2" nucleic acid or its complement under low stringency conditions,

- (xxxii) "Similar to CGI-135 protein" (SEQ ID No:268) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to CGI-135 protein" encoded by a nucleic acid that hybridizes to the "Similar to CGI-135 protein" nucleic acid or its complement under low stringency conditions,
- (xxxiii) "Sterile alpha and HEAT/Armadillo motif protein" (SEQ ID No:269) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sterile alpha and HEAT/Armadillo motif protein" encoded by a nucleic acid that hybridizes to the "Sterile alpha and HEAT/Armadillo motif protein" nucleic acid or its complement under low stringency conditions,
- (xxxiv) "Thioredoxin domain-containing protein" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions,
- (xxxv) "Vacuolar ATP synthase membrane sector associated protein m8-9" (SEQ ID No:273) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Vacuolar ATP synthase membrane sector associated protein m8-9" encoded by a nucleic acid that hybridizes to the "Vacuolar ATP synthase membrane sector associated protein m8-9" nucleic acid or its complement under low stringency conditions,
- (xxxvi) "Y391\_HUMAN" (SEQ ID No:274) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Y391\_HUMAN" encoded by a nucleic acid that hybridizes to the "Y391\_HUMAN" nucleic acid or its complement under low stringency conditions,
- (xxxvii) "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" (SEQ ID No:275) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" nucleic acid or its complement under low stringency conditions,
- (xxxviii) "hypothetical protein MGC22916" (SEQ ID No:276) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC22916" encoded by a nucleic acid that hybridizes to

the "hypothetical protein MGC22916" nucleic acid or its complement under low stringency conditions,

(xxxix) "integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "integral membrane transporter protein" nucleic acid or its complement under low stringency conditions, and/or

(xl) "tegt: testis enhanced gene transcript (bax inhibitor 1)" (SEQ ID No:278) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "tegt: testis enhanced gene transcript (bax inhibitor 1)" encoded by a nucleic acid that hybridizes to the "tegt: testis enhanced gene transcript (bax inhibitor 1)" nucleic acid or its complement under low stringency conditions, comprising the steps of

(a) exposing said complex, or a cell or organism containing same to one or more candidate molecules; and

(b) determining whether said candidate molecule is bound to the complex or protein.

26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 - 8 comprising the steps of (a) exposing said complex, or a cell or organism containing Aph-1a complex to one or more candidate molecules; and

(b) determining the amount of activity of protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.

27. The method of No. 26, wherein the amount of said complex is determined.

28. The method of No. 26, wherein the activity of said complex is determined.

29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining the processing of said substrate is modified in the presence of said candidate molecule.

30. The method of No. 26, wherein the amount of the individual protein components of said complex are determined.

31. The method of No. 30, wherein said determining step comprises determining whether  
(i) "18 kDa microsomal signal peptidase subunit " (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "18 kDa microsomal signal peptidase subunit " encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit " nucleic acid or its complement under low stringency conditions, and/or

(ii) "23 kDa microsomal signal peptidase" (SEQ ID No:221) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "23 kDa microsomal signal peptidase" encoded by a nucleic acid that hybridizes to the "23 kDa microsomal signal peptidase" nucleic acid or its complement under low stringency conditions, and/or

(iii) "25 kDa microsomal signal peptidase subunit" (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "25 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "25 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions, and/or

(iv) "ABCC1" (SEQ ID No:222) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ABCC1" encoded by a nucleic acid that hybridizes to the "ABCC1" nucleic acid or its complement under low stringency conditions, and/or

- (v) "APLP2" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions, and/or
- (vi) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions, and/or
- (vii) "ATM" (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATM" encoded by a nucleic acid that hybridizes to the "ATM" nucleic acid or its complement under low stringency conditions, and/or
- (viii) "ATP-binding cassette, sub-family A member 3" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family A member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A member 3" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "ATP1B1" (SEQ ID No:223) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP1B1" encoded by a nucleic acid that hybridizes to the "ATP1B1" nucleic acid or its complement under low stringency conditions, and/or
- (x) "ATP2C1" (SEQ ID No:224) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP2C1" encoded by a nucleic acid that hybridizes to the "ATP2C1" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "Acetolactate synthase homolog" (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Acetolactate synthase homolog" encoded by a nucleic acid that hybridizes to the "Acetolactate synthase homolog" nucleic acid or its complement under low stringency conditions, and/or
- (xii) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions, and/or

- (xiii) "Brain-specific GTP-binding protein" (SEQ ID No:225) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Brain-specific GTP-binding protein" encoded by a nucleic acid that hybridizes to the "Brain-specific GTP-binding protein" nucleic acid or its complement under low stringency conditions, and/or
- (xiv) "CDW92" (SEQ ID No:226) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDW92" encoded by a nucleic acid that hybridizes to the "CDW92" nucleic acid or its complement under low stringency conditions, and/or
- (xv) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions, and/or
- (xvi) "CNTNAP1" (SEQ ID No:227) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CNTNAP1" encoded by a nucleic acid that hybridizes to the "CNTNAP1" nucleic acid or its complement under low stringency conditions, and/or
- (xvii) "Cerebral protein-10" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cerebral protein-10" encoded by a nucleic acid that hybridizes to the "Cerebral protein-10" nucleic acid or its complement under low stringency conditions, and/or
- (xviii) "DNM1" (SEQ ID No:228) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DNM1" encoded by a nucleic acid that hybridizes to the "DNM1" nucleic acid or its complement under low stringency conditions, and/or
- (xix) "Dihydrofolate reductase" (SEQ ID No:229) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dihydrofolate reductase" encoded by a nucleic acid that hybridizes to the "Dihydrofolate reductase" nucleic acid or its complement under low stringency conditions, and/or
- (xx) "ENG" (SEQ ID No:230) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENG" encoded by a nucleic acid that hybridizes to the "ENG" nucleic acid or its complement under low stringency conditions, and/or



(xxi) "EXT2" (SEQ ID No:231) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EXT2" encoded by a nucleic acid that hybridizes to the "EXT2" nucleic acid or its complement under low stringency conditions, and/or

(xxii) "EXTL3" (SEQ ID No:232) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EXTL3" encoded by a nucleic acid that hybridizes to the "EXTL3" nucleic acid or its complement under low stringency conditions, and/or

(xxiii) "Endocytic receptor Endo180" (SEQ ID No:233) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Endocytic receptor Endo180" encoded by a nucleic acid that hybridizes to the "Endocytic receptor Endo180" nucleic acid or its complement under low stringency conditions, and/or

(xxiv) "FLJ13660" (SEQ ID No:234) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13660" encoded by a nucleic acid that hybridizes to the "FLJ13660" nucleic acid or its complement under low stringency conditions, and/or

(xxv) "GPR49" (SEQ ID No:235) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GPR49" encoded by a nucleic acid that hybridizes to the "GPR49" nucleic acid or its complement under low stringency conditions, and/or

(xxvi) "HK2" (SEQ ID No:236) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HK2" encoded by a nucleic acid that hybridizes to the "HK2" nucleic acid or its complement under low stringency conditions, and/or

(xxvii) "HU-K4" (SEQ ID No:133) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HU-K4" encoded by a nucleic acid that hybridizes to the "HU-K4" nucleic acid or its complement under low stringency conditions, and/or

(xxviii) "HUNC18a" (SEQ ID No:54) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HUNC18a" encoded by a nucleic acid that hybridizes to the "HUNC18a" nucleic acid or its complement under low stringency conditions, and/or

(xxix) "HYPOTHETICAL PROTEIN " (SEQ ID No:237) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN " encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN " nucleic acid or its complement under low stringency conditions, and/or

(xxx) "Hypothetical protein (Fragment)" (SEQ ID No:238) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein (Fragment)" encoded by a nucleic acid that hybridizes to the "Hypothetical protein (Fragment)" nucleic acid or its complement under low stringency conditions, and/or

(xxxi) "Hypothetical protein FLJ14562" (SEQ ID No:239) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ14562" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ14562" nucleic acid or its complement under low stringency conditions, and/or

(xxxii) "Hypothetical protein FLJ23630" (SEQ ID No:240) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ23630" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ23630" nucleic acid or its complement under low stringency conditions, and/or

(xxxiii) "Hypothetical protein KIAA0372" (SEQ ID No:241) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0372" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0372" nucleic acid or its complement under low stringency conditions, and/or

(xxxiv) "ICAM2" (SEQ ID No:200) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ICAM2" encoded by a nucleic acid that hybridizes to the "ICAM2" nucleic acid or its complement under low stringency conditions, and/or

(xxxv) "IGF2R" (SEQ ID No:242) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IGF2R" encoded by a nucleic acid that hybridizes to the "IGF2R" nucleic acid or its complement under low stringency conditions, and/or

(xxxvi) "ITPR1" (SEQ ID No:243) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITPR1" encoded by a nucleic acid that hybridizes to the "ITPR1" nucleic acid or its complement under low stringency conditions, and/or

(xxxvii) "Insulinoma-glucagonoma protein 20" (SEQ ID No:58) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Insulinoma-glucagonoma protein 20" encoded by a nucleic acid that hybridizes to the "Insulinoma-glucagonoma protein 20" nucleic acid or its complement under low stringency conditions, and/or

(xxxviii) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions, and/or

(xxxix) "KIAA0062 (FRAGMENT)" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0062 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0062 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or

(xl) "KIAA0251 (FRAGMENT)" (SEQ ID No:244) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0251 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0251 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or

(xli) "KIAA0363 (FRAGMENT)" (SEQ ID No:245) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0363 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0363 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or

(xlii) "KIAA0763" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions, and/or

(xliii) "KIAA0971" (SEQ ID No:246) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0971" encoded by a nucleic acid that hybridizes to the "KIAA0971" nucleic acid or its complement under low stringency conditions, and/or

(xlv) "KIAA1250" (SEQ ID No:247) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1250" encoded by a nucleic acid that hybridizes to the "KIAA1250" nucleic acid or its complement under low stringency conditions, and/or

(xlv) "LRP5" (SEQ ID No:248) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LRP5" encoded by a nucleic acid that hybridizes to the "LRP5" nucleic acid or its complement under low stringency conditions, and/or

(xlvi) "MGC4248 " (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4248 " encoded by a nucleic acid that hybridizes to the "MGC4248 " nucleic acid or its complement under low stringency conditions, and/or

(xlvii) "Mesenchymal stem cell protein DSCD75" (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Mesenchymal stem cell protein DSCD75" encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75" nucleic acid or its complement under low stringency conditions, and/or

(xlviii) "NRP2" (SEQ ID No:249) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NRP2" encoded by a nucleic acid that hybridizes to the "NRP2" nucleic acid or its complement under low stringency conditions, and/or

(xlix) "Neurotrypsin" (SEQ ID No:206) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions, and/or

(l) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions, and/or

(li) "PCDHA10" (SEQ ID No:250) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHA10" encoded by a nucleic acid that hybridizes to the "PCDHA10" nucleic acid or its complement under low stringency conditions, and/or

- (lii) "PCDHB12" (SEQ ID No:251) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB12" encoded by a nucleic acid that hybridizes to the "PCDHB12" nucleic acid or its complement under low stringency conditions, and/or
- (liii) "PCDHB13: protocadherin beta 13" (SEQ ID No:252) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB13: protocadherin beta 13" encoded by a nucleic acid that hybridizes to the "PCDHB13: protocadherin beta 13" nucleic acid or its complement under low stringency conditions, and/or
- (liv) "PCDHB4" (SEQ ID No:253) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB4" encoded by a nucleic acid that hybridizes to the "PCDHB4" nucleic acid or its complement under low stringency conditions, and/or
- (lv) "PCDHGB1" (SEQ ID No:254) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHGB1" encoded by a nucleic acid that hybridizes to the "PCDHGB1" nucleic acid or its complement under low stringency conditions, and/or
- (lvi) "PCDHGB6" (SEQ ID No:255) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHGB6" encoded by a nucleic acid that hybridizes to the "PCDHGB6" nucleic acid or its complement under low stringency conditions, and/or
- (lvii) "PMPCB" (SEQ ID No:256) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PMPCB" encoded by a nucleic acid that hybridizes to the "PMPCB" nucleic acid or its complement under low stringency conditions, and/or
- (lviii) "PP2C gamma" (SEQ ID No:257) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PP2C gamma" encoded by a nucleic acid that hybridizes to the "PP2C gamma" nucleic acid or its complement under low stringency conditions, and/or
- (lix) "Pcdhb17" (SEQ ID No:258) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pcdhb17" encoded by a nucleic acid that hybridizes to the "Pcdhb17" nucleic acid or its complement under low stringency conditions, and/or

- (lx) "Pen-2" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions, and/or
- (lxi) "Presenilin 1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions, and/or
- (lxii) "Presenilin 2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions, and/or
- (lxiii) "Protocadherin 7" (SEQ ID No:259) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin 7" encoded by a nucleic acid that hybridizes to the "Protocadherin 7" nucleic acid or its complement under low stringency conditions, and/or
- (lxiv) "Protocadherin beta 16" (SEQ ID No:260) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 16" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 16" nucleic acid or its complement under low stringency conditions, and/or
- (lxv) "Protocadherin beta 8" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 8" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8" nucleic acid or its complement under low stringency conditions, and/or
- (lxvi) "RAB-18" (SEQ ID No:261) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB-18" encoded by a nucleic acid that hybridizes to the "RAB-18" nucleic acid or its complement under low stringency conditions, and/or
- (lxvii) "RNASEL" (SEQ ID No:262) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RNASEL" encoded by a nucleic acid that hybridizes to the "RNASEL" nucleic acid or its complement under low stringency conditions, and/or
- (lxviii) "Rab3 GTPase-activating protein, non-catalytic subunit" (SEQ ID No:263) or a functionally active derivative thereof, or a functionally active fragment thereof, or a

homolog thereof, or a variant of "Rab3 GTPase-activating protein, non-catalytic subunit" encoded by a nucleic acid that hybridizes to the "Rab3 GTPase-activating protein, non-catalytic subunit" nucleic acid or its complement under low stringency conditions, and/or (lxi) "Retinal short-chain dehydrogenase/reductase retSDR2" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2" encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2" nucleic acid or its complement under low stringency conditions, and/or

(lxx) "SMAP-1B" (SEQ ID No:264) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SMAP-1B" encoded by a nucleic acid that hybridizes to the "SMAP-1B" nucleic acid or its complement under low stringency conditions, and/or

(lxxi) "SPTLC2" (SEQ ID No:265) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SPTLC2" encoded by a nucleic acid that hybridizes to the "SPTLC2" nucleic acid or its complement under low stringency conditions, and/or

(lxxii) "STMN3" (SEQ ID No:87) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STMN3" encoded by a nucleic acid that hybridizes to the "STMN3" nucleic acid or its complement under low stringency conditions, and/or

(lxxiii) "Sideroflexin 1" (SEQ ID No:266) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sideroflexin 1" encoded by a nucleic acid that hybridizes to the "Sideroflexin 1" nucleic acid or its complement under low stringency conditions, and/or

(lxxiv) "Signal transducer and activator of transcription-1" (SEQ ID No:267) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Signal transducer and activator of transcription-1" encoded by a nucleic acid that hybridizes to the "Signal transducer and activator of transcription-1" nucleic acid or its complement under low stringency conditions, and/or

(lxxv) "Similar to CGI-135 protein" (SEQ ID No:268) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to CGI-135 protein" encoded by a nucleic acid that hybridizes to the "Similar to CGI-135 protein" nucleic acid or its complement under low stringency conditions, and/or

(lxxvi) "Sterile alpha and HEAT/Armadillo motif protein" (SEQ ID No:269) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sterile alpha and HEAT/Armadillo motif protein" encoded by a nucleic acid that hybridizes to the "Sterile alpha and HEAT/Armadillo motif protein" nucleic acid or its complement under low stringency conditions, and/or

(lxxvii) "Sterol O-acyltransferase 1" (SEQ ID No:270) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sterol O-acyltransferase 1" encoded by a nucleic acid that hybridizes to the "Sterol O-acyltransferase 1" nucleic acid or its complement under low stringency conditions, and/or

(lxxviii) "Thioredoxin domain-containing protein" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions, and/or

(lxxix) "Triple functional domain protein (PTPRF interacting)" (SEQ ID No:271) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Triple functional domain protein (PTPRF interacting)" encoded by a nucleic acid that hybridizes to the "Triple functional domain protein (PTPRF interacting)" nucleic acid or its complement under low stringency conditions, and/or

(lxxx) "UNC5C" (SEQ ID No:272) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "UNC5C" encoded by a nucleic acid that hybridizes to the "UNC5C" nucleic acid or its complement under low stringency conditions, and/or

(lxxxi) "Vacuolar ATP synthase membrane sector associated protein m8-9" (SEQ ID No:273) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Vacuolar ATP synthase membrane sector associated protein m8-9" encoded by a nucleic acid that hybridizes to the "Vacuolar ATP synthase membrane sector associated protein m8-9" nucleic acid or its complement under low stringency conditions, and/or

(lxxxii) "Y391\_HUMAN" (SEQ ID No:274) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Y391\_HUMAN" encoded by a nucleic acid that hybridizes to the "Y391\_HUMAN" nucleic acid or its complement under low stringency conditions, and/or



(lxxxiii) "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" (SEQ ID No:275) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" nucleic acid or its complement under low stringency conditions, and/or

(lxxxiv) "hypothetical protein MGC22916" (SEQ ID No:276) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC22916" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC22916" nucleic acid or its complement under low stringency conditions, and/or

(lxxxv) "integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "integral membrane transporter protein" nucleic acid or its complement under low stringency conditions, and/or

(lxxxvi) "tegt: testis enhanced gene transcript (bax inhibitor 1)" (SEQ ID No:278) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "tegt: testis enhanced gene transcript (bax inhibitor 1)" encoded by a nucleic acid that hybridizes to the "tegt: testis enhanced gene transcript (bax inhibitor 1)" nucleic acid or its complement under low stringency conditions, and/or

(lxxxvii) "vacuolar protein sorting protein 18" (SEQ ID No:279) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "vacuolar protein sorting protein 18" encoded by a nucleic acid that hybridizes to the "vacuolar protein sorting protein 18" nucleic acid or its complement under low stringency conditions, is present in the complex.

32. The method of any of No. 26 - 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 - 8 for the manufacture of a medicament

for the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

34. A method for the production of a pharmaceutical composition comprising carrying out the method of any of No. 1 - 8 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.

35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, activity of, or component composition of, or intracellular localization of the complex of any one of the No. 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in an analogous sample from a subject not having the disease or disorder or predisposition indicates the presence in the subject of the disease or disorder or predisposition in the subject.

36. The method of No. 35, wherein the amount of said complex is determined.

37. The method of No. 35, wherein the activity of said complex is determined.

38. The method of No. 37, wherein said determining step comprises isolating from the subject said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.

39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.

40. The method of No. 39, wherein said determining step comprises determining whether (i) "18 kDa microsomal signal peptidase subunit " (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "18 kDa microsomal signal peptidase subunit " encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit " nucleic acid or its complement under low stringency conditions, and/or

(ii) "23 kDa microsomal signal peptidase" (SEQ ID No:221) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "23 kDa microsomal signal peptidase" encoded by a nucleic acid that hybridizes to the "23 kDa microsomal signal peptidase" nucleic acid or its complement under low stringency conditions, and/or

(iii) "25 kDa microsomal signal peptidase subunit" (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "25 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "25 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions, and/or

(iv) "ABCC1" (SEQ ID No:222) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ABCC1" encoded by a nucleic acid that hybridizes to the "ABCC1" nucleic acid or its complement under low stringency conditions, and/or

(v) "APLP2" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions, and/or

(vi) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions, and/or

(vii) "ATM" (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATM" encoded by a nucleic acid that hybridizes to the "ATM" nucleic acid or its complement under low stringency conditions, and/or

- (viii) "ATP-binding cassette, sub-family A member 3" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family A member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A member 3" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "ATP1B1" (SEQ ID No:223) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP1B1" encoded by a nucleic acid that hybridizes to the "ATP1B1" nucleic acid or its complement under low stringency conditions, and/or
- (x) "ATP2C1" (SEQ ID No:224) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP2C1" encoded by a nucleic acid that hybridizes to the "ATP2C1" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "Acetolactate synthase homolog" (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Acetolactate synthase homolog" encoded by a nucleic acid that hybridizes to the "Acetolactate synthase homolog" nucleic acid or its complement under low stringency conditions, and/or
- (xii) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions, and/or
- (xiii) "Brain-specific GTP-binding protein" (SEQ ID No:225) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Brain-specific GTP-binding protein" encoded by a nucleic acid that hybridizes to the "Brain-specific GTP-binding protein" nucleic acid or its complement under low stringency conditions, and/or
- (xiv) "CDW92" (SEQ ID No:226) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDW92" encoded by a nucleic acid that hybridizes to the "CDW92" nucleic acid or its complement under low stringency conditions, and/or
- (xv) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a

nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions, and/or

(xvi) "CNTNAP1" (SEQ ID No:227) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CNTNAP1" encoded by a nucleic acid that hybridizes to the "CNTNAP1" nucleic acid or its complement under low stringency conditions, and/or

(xvii) "Cerebral protein-10" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cerebral protein-10" encoded by a nucleic acid that hybridizes to the "Cerebral protein-10" nucleic acid or its complement under low stringency conditions, and/or

(xviii) "DNM1" (SEQ ID No:228) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DNM1" encoded by a nucleic acid that hybridizes to the "DNM1" nucleic acid or its complement under low stringency conditions, and/or

(xix) "Dihydrofolate reductase" (SEQ ID No:229) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dihydrofolate reductase" encoded by a nucleic acid that hybridizes to the "Dihydrofolate reductase" nucleic acid or its complement under low stringency conditions, and/or

(xx) "ENG" (SEQ ID No:230) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENG" encoded by a nucleic acid that hybridizes to the "ENG" nucleic acid or its complement under low stringency conditions, and/or

(xxi) "EXT2" (SEQ ID No:231) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EXT2" encoded by a nucleic acid that hybridizes to the "EXT2" nucleic acid or its complement under low stringency conditions, and/or

(xxii) "EXTL3" (SEQ ID No:232) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EXTL3" encoded by a nucleic acid that hybridizes to the "EXTL3" nucleic acid or its complement under low stringency conditions, and/or

(xxiii) "Endocytic receptor Endo180" (SEQ ID No:233) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Endocytic receptor Endo180" encoded by a nucleic acid that hybridizes to the

"Endocytic receptor Endo180" nucleic acid or its complement under low stringency conditions, and/or

(xxiv) "FLJ13660" (SEQ ID No:234) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13660" encoded by a nucleic acid that hybridizes to the "FLJ13660" nucleic acid or its complement under low stringency conditions, and/or

(xxv) "GPR49" (SEQ ID No:235) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GPR49" encoded by a nucleic acid that hybridizes to the "GPR49" nucleic acid or its complement under low stringency conditions, and/or

(xxvi) "HK2" (SEQ ID No:236) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HK2" encoded by a nucleic acid that hybridizes to the "HK2" nucleic acid or its complement under low stringency conditions, and/or

(xxvii) "HU-K4" (SEQ ID No:133) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HU-K4" encoded by a nucleic acid that hybridizes to the "HU-K4" nucleic acid or its complement under low stringency conditions, and/or

(xxviii) "HUNC18a" (SEQ ID No:54) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HUNC18a" encoded by a nucleic acid that hybridizes to the "HUNC18a" nucleic acid or its complement under low stringency conditions, and/or

(xxix) "HYPOTHETICAL PROTEIN " (SEQ ID No:237) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN " encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN " nucleic acid or its complement under low stringency conditions, and/or

(xxx) "Hypothetical protein (Fragment)" (SEQ ID No:238) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein (Fragment)" encoded by a nucleic acid that hybridizes to the "Hypothetical protein (Fragment)" nucleic acid or its complement under low stringency conditions, and/or

(xxxi) "Hypothetical protein FLJ14562" (SEQ ID No:239) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a

variant of "Hypothetical protein FLJ14562" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ14562" nucleic acid or its complement under low stringency conditions, and/or

(xxxii) "Hypothetical protein FLJ23630" (SEQ ID No:240) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ23630" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ23630" nucleic acid or its complement under low stringency conditions, and/or

(xxxiii) "Hypothetical protein KIAA0372" (SEQ ID No:241) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0372" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0372" nucleic acid or its complement under low stringency conditions, and/or

(xxxiv) "ICAM2" (SEQ ID No:200) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ICAM2" encoded by a nucleic acid that hybridizes to the "ICAM2" nucleic acid or its complement under low stringency conditions, and/or

(xxxv) "IGF2R" (SEQ ID No:242) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IGF2R" encoded by a nucleic acid that hybridizes to the "IGF2R" nucleic acid or its complement under low stringency conditions, and/or

(xxxvi) "ITPR1" (SEQ ID No:243) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITPR1" encoded by a nucleic acid that hybridizes to the "ITPR1" nucleic acid or its complement under low stringency conditions, and/or

(xxxvii) "Insulinoma-glucagonoma protein 20" (SEQ ID No:58) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Insulinoma-glucagonoma protein 20" encoded by a nucleic acid that hybridizes to the "Insulinoma-glucagonoma protein 20" nucleic acid or its complement under low stringency conditions, and/or

(xxxviii) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that

hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions, and/or

(xxxix) "KIAA0062 (FRAGMENT)" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0062 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0062 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or

(xl) "KIAA0251 (FRAGMENT)" (SEQ ID No:244) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0251 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0251 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or

(xli) "KIAA0363 (FRAGMENT)" (SEQ ID No:245) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0363 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0363 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or

(xlii) "KIAA0763" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions, and/or

(xliii) "KIAA0971" (SEQ ID No:246) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0971" encoded by a nucleic acid that hybridizes to the "KIAA0971" nucleic acid or its complement under low stringency conditions, and/or

(xliv) "KIAA1250" (SEQ ID No:247) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1250" encoded by a nucleic acid that hybridizes to the "KIAA1250" nucleic acid or its complement under low stringency conditions, and/or

(xlv) "LRP5" (SEQ ID No:248) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LRP5" encoded by a nucleic acid that hybridizes to the "LRP5" nucleic acid or its complement under low stringency conditions, and/or

(xlvi) "MGC4248 " (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4248 " encoded by a nucleic acid that hybridizes to the "MGC4248 " nucleic acid or its complement under low stringency conditions, and/or



(xlvii) "Mesenchymal stem cell protein DSCD75" (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Mesenchymal stem cell protein DSCD75" encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75" nucleic acid or its complement under low stringency conditions, and/or

(xlviii) "NRP2" (SEQ ID No:249) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NRP2" encoded by a nucleic acid that hybridizes to the "NRP2" nucleic acid or its complement under low stringency conditions, and/or

(xlix) "Neurotrypsin" (SEQ ID No:206) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions, and/or

(l) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions, and/or

(li) "PCDHA10" (SEQ ID No:250) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHA10" encoded by a nucleic acid that hybridizes to the "PCDHA10" nucleic acid or its complement under low stringency conditions, and/or

(lii) "PCDHB12" (SEQ ID No:251) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB12" encoded by a nucleic acid that hybridizes to the "PCDHB12" nucleic acid or its complement under low stringency conditions, and/or

(liii) "PCDHB13: protocadherin beta 13" (SEQ ID No:252) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB13: protocadherin beta 13" encoded by a nucleic acid that hybridizes to the "PCDHB13: protocadherin beta 13" nucleic acid or its complement under low stringency conditions, and/or

(liv) "PCDHB4" (SEQ ID No:253) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB4" encoded by a nucleic acid that hybridizes to the "PCDHB4" nucleic acid or its complement under low stringency conditions, and/or

- (iv) "PCDHGB1" (SEQ ID No:254) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHGB1" encoded by a nucleic acid that hybridizes to the "PCDHGB1" nucleic acid or its complement under low stringency conditions, and/or
- (lvi) "PCDHGB6" (SEQ ID No:255) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHGB6" encoded by a nucleic acid that hybridizes to the "PCDHGB6" nucleic acid or its complement under low stringency conditions, and/or
- (lvii) "PMPCB" (SEQ ID No:256) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PMPCB" encoded by a nucleic acid that hybridizes to the "PMPCB" nucleic acid or its complement under low stringency conditions, and/or
- (lviii) "PP2C gamma" (SEQ ID No:257) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PP2C gamma" encoded by a nucleic acid that hybridizes to the "PP2C gamma" nucleic acid or its complement under low stringency conditions, and/or
- (lix) "Pcdhb17" (SEQ ID No:258) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pcdhb17" encoded by a nucleic acid that hybridizes to the "Pcdhb17" nucleic acid or its complement under low stringency conditions, and/or
- (lx) "Pen-2" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions, and/or
- (lxi) "Presenilin 1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions, and/or
- (lxii) "Presenilin 2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions, and/or
- (lxiii) "Protocadherin 7" (SEQ ID No:259) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin

7" encoded by a nucleic acid that hybridizes to the "Protocadherin 7" nucleic acid or its complement under low stringency conditions, and/or

(lxiv) "Protocadherin beta 16" (SEQ ID No:260) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"Protocadherin beta 16" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 16" nucleic acid or its complement under low stringency conditions, and/or

(lxv) "Protocadherin beta 8" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"Protocadherin beta 8" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8" nucleic acid or its complement under low stringency conditions, and/or

(lxvi) "RAB-18" (SEQ ID No:261) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB-18" encoded by a nucleic acid that hybridizes to the "RAB-18" nucleic acid or its complement under low stringency conditions, and/or

(lxvii) "RNASEL" (SEQ ID No:262) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RNASEL" encoded by a nucleic acid that hybridizes to the "RNASEL" nucleic acid or its complement under low stringency conditions, and/or

(lxviii) "Rab3 GTPase-activating protein, non-catalytic subunit" (SEQ ID No:263) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Rab3 GTPase-activating protein, non-catalytic subunit" encoded by a nucleic acid that hybridizes to the "Rab3 GTPase-activating protein, non-catalytic subunit" nucleic acid or its complement under low stringency conditions, and/or

(lxix) "Retinal short-chain dehydrogenase/reductase retSDR2" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2" encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2" nucleic acid or its complement under low stringency conditions, and/or

(lxx) "SMAP-1B" (SEQ ID No:264) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SMAP-1B" encoded by a nucleic acid that hybridizes to the "SMAP-1B" nucleic acid or its complement under low stringency conditions, and/or

(lxxi) "SPTLC2" (SEQ ID No:265) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SPTLC2" encoded by a nucleic acid that hybridizes to the "SPTLC2" nucleic acid or its complement under low stringency conditions, and/or

(lxxii) "STMN3" (SEQ ID No:87) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STMN3" encoded by a nucleic acid that hybridizes to the "STMN3" nucleic acid or its complement under low stringency conditions, and/or

(lxxiii) "Sideroflexin 1" (SEQ ID No:266) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sideroflexin 1" encoded by a nucleic acid that hybridizes to the "Sideroflexin 1" nucleic acid or its complement under low stringency conditions, and/or

(lxxiv) "Signal transducer and activator of transcription-1" (SEQ ID No:267) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Signal transducer and activator of transcription-1" encoded by a nucleic acid that hybridizes to the "Signal transducer and activator of transcription-1" nucleic acid or its complement under low stringency conditions, and/or

(lxxv) "Similar to CGI-135 protein" (SEQ ID No:268) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to CGI-135 protein" encoded by a nucleic acid that hybridizes to the "Similar to CGI-135 protein" nucleic acid or its complement under low stringency conditions, and/or

(lxxvi) "Sterile alpha and HEAT/Armadillo motif protein" (SEQ ID No:269) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sterile alpha and HEAT/Armadillo motif protein" encoded by a nucleic acid that hybridizes to the "Sterile alpha and HEAT/Armadillo motif protein" nucleic acid or its complement under low stringency conditions, and/or

(lxxvii) "Sterol O-acyltransferase 1" (SEQ ID No:270) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sterol O-acyltransferase 1" encoded by a nucleic acid that hybridizes to the "Sterol O-acyltransferase 1" nucleic acid or its complement under low stringency conditions, and/or

(lxxviii) "Thioredoxin domain-containing protein" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that

hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions, and/or

(lxxix) "Triple functional domain protein (PTPRF interacting)" (SEQ ID No:271) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Triple functional domain protein (PTPRF interacting)" encoded by a nucleic acid that hybridizes to the "Triple functional domain protein (PTPRF interacting)" nucleic acid or its complement under low stringency conditions, and/or

(lxxx) "UNC5C" (SEQ ID No:272) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "UNC5C" encoded by a nucleic acid that hybridizes to the "UNC5C" nucleic acid or its complement under low stringency conditions, and/or

(lxxxi) "Vacuolar ATP synthase membrane sector associated protein m8-9" (SEQ ID No:273) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Vacuolar ATP synthase membrane sector associated protein m8-9" encoded by a nucleic acid that hybridizes to the "Vacuolar ATP synthase membrane sector associated protein m8-9" nucleic acid or its complement under low stringency conditions, and/or

(lxxxii) "Y391\_HUMAN" (SEQ ID No:274) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Y391\_HUMAN" encoded by a nucleic acid that hybridizes to the "Y391\_HUMAN" nucleic acid or its complement under low stringency conditions, and/or

(lxxxiii) "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" (SEQ ID No:275) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" nucleic acid or its complement under low stringency conditions, and/or

(lxxxiv) "hypothetical protein MGC22916" (SEQ ID No:276) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC22916" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC22916" nucleic acid or its complement under low stringency conditions, and/or

(lxxxv) "integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "integral membrane transporter protein" nucleic acid or its complement under low stringency conditions, and/or

(lxxxvi) "tegt: testis enhanced gene transcript (bax inhibitor 1)" (SEQ ID No:278) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "tegt: testis enhanced gene transcript (bax inhibitor 1)" encoded by a nucleic acid that hybridizes to the "tegt: testis enhanced gene transcript (bax inhibitor 1)" nucleic acid or its complement under low stringency conditions, and/or

(lxxxvii) "vacuolar protein sorting protein 18" (SEQ ID No:279) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "vacuolar protein sorting protein 18" encoded by a nucleic acid that hybridizes to the "vacuolar protein sorting protein 18" nucleic acid or its complement under low stringency conditions, is present in the complex.

41. The complex of any one of No. 1 - 8, or proteins of No. 13 or the antibody or fragment of No. 17, for use in a method of diagnosing a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity or component composition of or intracellular localization of, the complex of anyone of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of

RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), or protein components of, said complex.

43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.

44. The method according to No. 42, wherein said disease or disorder involves increased levels of the amount or activity of said complex.

45. Complex of any of No. 1 - 8 and/or protein selected from the following proteins  
(i) "18 kDa microsomal signal peptidase subunit" (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "18 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,

(ii) "23 kDa microsomal signal peptidase" (SEQ ID No:221) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "23 kDa microsomal signal peptidase" encoded by a nucleic acid that hybridizes to the "23 kDa microsomal signal peptidase" nucleic acid or its complement under low stringency conditions,

(iii) "25 kDa microsomal signal peptidase subunit" (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "25 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "25 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,

(iv) "ABCC1" (SEQ ID No:222) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ABCC1" encoded by a nucleic acid that hybridizes to the "ABCC1" nucleic acid or its complement under low stringency conditions,

(v) "APLP2" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a

nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions,

(vi) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,

(vii) "ATM" (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATM" encoded by a nucleic acid that hybridizes to the "ATM" nucleic acid or its complement under low stringency conditions,

(viii) "ATP-binding cassette, sub-family A member 3" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family A member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A member 3" nucleic acid or its complement under low stringency conditions,

(ix) "ATP1B1" (SEQ ID No:223) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP1B1" encoded by a nucleic acid that hybridizes to the "ATP1B1" nucleic acid or its complement under low stringency conditions,

(x) "ATP2C1" (SEQ ID No:224) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP2C1" encoded by a nucleic acid that hybridizes to the "ATP2C1" nucleic acid or its complement under low stringency conditions,

(xi) "Acetolactate synthase homolog" (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Acetolactate synthase homolog" encoded by a nucleic acid that hybridizes to the "Acetolactate synthase homolog" nucleic acid or its complement under low stringency conditions,

(xii) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,

(xiii) "Brain-specific GTP-binding protein" (SEQ ID No:225) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a



variant of "Brain-specific GTP-binding protein" encoded by a nucleic acid that hybridizes to the "Brain-specific GTP-binding protein" nucleic acid or its complement under low stringency conditions,

(xiv) "CDW92" (SEQ ID No:226) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDW92" encoded by a nucleic acid that hybridizes to the "CDW92" nucleic acid or its complement under low stringency conditions,

(xv) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,

(xvi) "CNTNAP1" (SEQ ID No:227) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CNTNAP1" encoded by a nucleic acid that hybridizes to the "CNTNAP1" nucleic acid or its complement under low stringency conditions,

(xvii) "Cerebral protein-10" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cerebral protein-10" encoded by a nucleic acid that hybridizes to the "Cerebral protein-10" nucleic acid or its complement under low stringency conditions,

(xviii) "DNM1" (SEQ ID No:228) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DNM1" encoded by a nucleic acid that hybridizes to the "DNM1" nucleic acid or its complement under low stringency conditions,

(xix) "Dihydrofolate reductase" (SEQ ID No:229) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dihydrofolate reductase" encoded by a nucleic acid that hybridizes to the "Dihydrofolate reductase" nucleic acid or its complement under low stringency conditions,

(xx) "ENG" (SEQ ID No:230) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENG" encoded by a nucleic acid that hybridizes to the "ENG" nucleic acid or its complement under low stringency conditions,

(xxi) "EXT2" (SEQ ID No:231) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EXT2" encoded by a

nucleic acid that hybridizes to the "EXT2" nucleic acid or its complement under low stringency conditions,

(xxii) "EXTL3" (SEQ ID No:232) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EXTL3" encoded by a nucleic acid that hybridizes to the "EXTL3" nucleic acid or its complement under low stringency conditions,

(xxiii) "Endocytic receptor Endo180" (SEQ ID No:233) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Endocytic receptor Endo180" encoded by a nucleic acid that hybridizes to the "Endocytic receptor Endo180" nucleic acid or its complement under low stringency conditions,

(xxiv) "FLJ13660" (SEQ ID No:234) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13660" encoded by a nucleic acid that hybridizes to the "FLJ13660" nucleic acid or its complement under low stringency conditions,

(xxv) "GPR49" (SEQ ID No:235) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GPR49" encoded by a nucleic acid that hybridizes to the "GPR49" nucleic acid or its complement under low stringency conditions,

(xxvi) "HK2" (SEQ ID No:236) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HK2" encoded by a nucleic acid that hybridizes to the "HK2" nucleic acid or its complement under low stringency conditions,

(xxvii) "HU-K4" (SEQ ID No:133) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HU-K4" encoded by a nucleic acid that hybridizes to the "HU-K4" nucleic acid or its complement under low stringency conditions,

(xxviii) "HUNC18a" (SEQ ID No:54) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HUNC18a" encoded by a nucleic acid that hybridizes to the "HUNC18a" nucleic acid or its complement under low stringency conditions,

(xxix) "HYPOTHETICAL PROTEIN " (SEQ ID No:237) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN " encoded by a nucleic acid that hybridizes to the

"HYPOTHETICAL PROTEIN " nucleic acid or its complement under low stringency conditions,

(xxx) "Hypothetical protein (Fragment)" (SEQ ID No:238) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein (Fragment)" encoded by a nucleic acid that hybridizes to the "Hypothetical protein (Fragment)" nucleic acid or its complement under low stringency conditions,

(xxxi) "Hypothetical protein FLJ14562" (SEQ ID No:239) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ14562" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ14562" nucleic acid or its complement under low stringency conditions,

(xxxii) "Hypothetical protein FLJ23630" (SEQ ID No:240) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ23630" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ23630" nucleic acid or its complement under low stringency conditions,

(xxxiii) "Hypothetical protein KIAA0372" (SEQ ID No:241) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0372" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0372" nucleic acid or its complement under low stringency conditions,

(xxxiv) "ICAM2" (SEQ ID No:200) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ICAM2" encoded by a nucleic acid that hybridizes to the "ICAM2" nucleic acid or its complement under low stringency conditions,

(xxxv) "IGF2R" (SEQ ID No:242) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IGF2R" encoded by a nucleic acid that hybridizes to the "IGF2R" nucleic acid or its complement under low stringency conditions,

(xxxvi) "ITPR1" (SEQ ID No:243) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITPR1" encoded by a nucleic acid that hybridizes to the "ITPR1" nucleic acid or its complement under low stringency conditions,

(xxxvii) "Insulinoma-glucagonoma protein 20" (SEQ ID No:58) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Insulinoma-glucagonoma protein 20" encoded by a nucleic acid that hybridizes to the "Insulinoma-glucagonoma protein 20" nucleic acid or its complement under low stringency conditions,

(xxxviii) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions,

(xxxix) "KIAA0062 (FRAGMENT)" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0062 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0062 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xl) "KIAA0251 (FRAGMENT)" (SEQ ID No:244) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0251 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0251 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xli) "KIAA0363 (FRAGMENT)" (SEQ ID No:245) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0363 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0363 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xlii) "KIAA0763" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions,

(xlili) "KIAA0971" (SEQ ID No:246) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0971" encoded by a nucleic acid that hybridizes to the "KIAA0971" nucleic acid or its complement under low stringency conditions,

(xliv) "KIAA1250" (SEQ ID No:247) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1250" encoded by a nucleic acid that hybridizes to the "KIAA1250" nucleic acid or its complement under low stringency conditions,

- (xlv) "LRP5" (SEQ ID No:248) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LRP5" encoded by a nucleic acid that hybridizes to the "LRP5" nucleic acid or its complement under low stringency conditions,
- (xlvi) "MGC4248 " (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4248 " encoded by a nucleic acid that hybridizes to the "MGC4248 " nucleic acid or its complement under low stringency conditions,
- (xlvii) "Mesenchymal stem cell protein DSCD75" (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Mesenchymal stem cell protein DSCD75" encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75" nucleic acid or its complement under low stringency conditions,
- (xlviii) "NRP2" (SEQ ID No:249) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NRP2" encoded by a nucleic acid that hybridizes to the "NRP2" nucleic acid or its complement under low stringency conditions,
- (xlix) "Neurotrypsin" (SEQ ID No:206) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions,
- (l) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,
- (li) "PCDHA10" (SEQ ID No:250) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHA10" encoded by a nucleic acid that hybridizes to the "PCDHA10" nucleic acid or its complement under low stringency conditions,
- (lii) "PCDHB12" (SEQ ID No:251) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB12" encoded by a nucleic acid that hybridizes to the "PCDHB12" nucleic acid or its complement under low stringency conditions,

- (liii) "PCDHB13: protocadherin beta 13" (SEQ ID No:252) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB13: protocadherin beta 13" encoded by a nucleic acid that hybridizes to the "PCDHB13: protocadherin beta 13" nucleic acid or its complement under low stringency conditions,
- (liv) "PCDHB4" (SEQ ID No:253) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB4" encoded by a nucleic acid that hybridizes to the "PCDHB4" nucleic acid or its complement under low stringency conditions,
- (lv) "PCDHGB1" (SEQ ID No:254) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHGB1" encoded by a nucleic acid that hybridizes to the "PCDHGB1" nucleic acid or its complement under low stringency conditions,
- (lvi) "PCDHGB6" (SEQ ID No:255) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHGB6" encoded by a nucleic acid that hybridizes to the "PCDHGB6" nucleic acid or its complement under low stringency conditions,
- (lvii) "PMPCB" (SEQ ID No:256) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PMPCB" encoded by a nucleic acid that hybridizes to the "PMPCB" nucleic acid or its complement under low stringency conditions,
- (lviii) "PP2C gamma" (SEQ ID No:257) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PP2C gamma" encoded by a nucleic acid that hybridizes to the "PP2C gamma" nucleic acid or its complement under low stringency conditions,
- (lix) "Pcdhb17" (SEQ ID No:258) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pcdhb17" encoded by a nucleic acid that hybridizes to the "Pcdhb17" nucleic acid or its complement under low stringency conditions,
- (lx) "Pen-2" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions,

- (lxi) "Presenilin 1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions,
- (lxii) "Presenilin 2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions,
- (lxiii) "Protocadherin 7" (SEQ ID No:259) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin 7" encoded by a nucleic acid that hybridizes to the "Protocadherin 7" nucleic acid or its complement under low stringency conditions,
- (lxiv) "Protocadherin beta 16" (SEQ ID No:260) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 16" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 16" nucleic acid or its complement under low stringency conditions,
- (lxv) "Protocadherin beta 8" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 8" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8" nucleic acid or its complement under low stringency conditions,
- (lxvi) "RAB-18" (SEQ ID No:261) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB-18" encoded by a nucleic acid that hybridizes to the "RAB-18" nucleic acid or its complement under low stringency conditions,
- (lxvii) "RNASEL" (SEQ ID No:262) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RNASEL" encoded by a nucleic acid that hybridizes to the "RNASEL" nucleic acid or its complement under low stringency conditions,
- (lxviii) "Rab3 GTPase-activating protein, non-catalytic subunit" (SEQ ID No:263) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Rab3 GTPase-activating protein, non-catalytic subunit" encoded by a nucleic acid that hybridizes to the "Rab3 GTPase-activating protein, non-catalytic subunit" nucleic acid or its complement under low stringency conditions,

(Ixxix) "Retinal short-chain dehydrogenase/reductase retSDR2" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2" encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2" nucleic acid or its complement under low stringency conditions,

(Ixx) "SMAP-1B" (SEQ ID No:264) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SMAP-1B" encoded by a nucleic acid that hybridizes to the "SMAP-1B" nucleic acid or its complement under low stringency conditions,

(Ixxi) "SPTLC2" (SEQ ID No:265) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SPTLC2" encoded by a nucleic acid that hybridizes to the "SPTLC2" nucleic acid or its complement under low stringency conditions,

(Ixxii) "STMN3" (SEQ ID No:87) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STMN3" encoded by a nucleic acid that hybridizes to the "STMN3" nucleic acid or its complement under low stringency conditions,

(Ixxiii) "Sideroflexin 1" (SEQ ID No:266) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sideroflexin 1" encoded by a nucleic acid that hybridizes to the "Sideroflexin 1" nucleic acid or its complement under low stringency conditions,

(Ixxiv) "Signal transducer and activator of transcription-1" (SEQ ID No:267) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Signal transducer and activator of transcription-1" encoded by a nucleic acid that hybridizes to the "Signal transducer and activator of transcription-1" nucleic acid or its complement under low stringency conditions,

(Ixxv) "Similar to CGI-135 protein" (SEQ ID No:268) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to CGI-135 protein" encoded by a nucleic acid that hybridizes to the "Similar to CGI-135 protein" nucleic acid or its complement under low stringency conditions,

(Ixxvi) "Sterile alpha and HEAT/Armadillo motif protein" (SEQ ID No:269) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sterile alpha and HEAT/Armadillo motif protein" encoded by a nucleic



acid that hybridizes to the "Sterile alpha and HEAT/Armadillo motif protein" nucleic acid or its complement under low stringency conditions,

(lxxvii) "Sterol O-acyltransferase 1" (SEQ ID No:270) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sterol O-acyltransferase 1" encoded by a nucleic acid that hybridizes to the "Sterol O-acyltransferase 1" nucleic acid or its complement under low stringency conditions,  
 (lxxviii) "Thioredoxin domain-containing protein" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions,

(lxxix) "Triple functional domain protein (PTPRF interacting)" (SEQ ID No:271) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Triple functional domain protein (PTPRF interacting)" encoded by a nucleic acid that hybridizes to the "Triple functional domain protein (PTPRF interacting)" nucleic acid or its complement under low stringency conditions,  
 (lxxx) "UNC5C" (SEQ ID No:272) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "UNC5C" encoded by a nucleic acid that hybridizes to the "UNC5C" nucleic acid or its complement under low stringency conditions,

(lxxxi) "Vacuolar ATP synthase membrane sector associated protein m8-9" (SEQ ID No:273) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Vacuolar ATP synthase membrane sector associated protein m8-9" encoded by a nucleic acid that hybridizes to the "Vacuolar ATP synthase membrane sector associated protein m8-9" nucleic acid or its complement under low stringency conditions,

(lxxxii) "Y391\_HUMAN" (SEQ ID No:274) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Y391\_HUMAN" encoded by a nucleic acid that hybridizes to the "Y391\_HUMAN" nucleic acid or its complement under low stringency conditions,

(lxxxiii) "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" (SEQ ID No:275) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" encoded by a nucleic acid that hybridizes to the

"hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" nucleic acid or its complement under low stringency conditions,

(lxxxiv) "hypothetical protein MGC22916" (SEQ ID No:276) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC22916" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC22916" nucleic acid or its complement under low stringency conditions,

(lxxxv) "integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "integral membrane transporter protein" nucleic acid or its complement under low stringency conditions,

(lxxxvi) "tegt: testis enhanced gene transcript (bax inhibitor 1)" (SEQ ID No:278) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "tegt: testis enhanced gene transcript (bax inhibitor 1)" encoded by a nucleic acid that hybridizes to the "tegt: testis enhanced gene transcript (bax inhibitor 1)" nucleic acid or its complement under low stringency conditions,

and/or(lxxxvii) "vacuolar protein sorting protein 18" (SEQ ID No:279) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "vacuolar protein sorting protein 18" encoded by a nucleic acid that hybridizes to the "vacuolar protein sorting protein 18" nucleic acid or its complement under low stringency conditions, as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

The present invention further relates to the following embodiments of the Pen-2.complex

1. A protein complex selected from complex (I) and comprising

(a) at least one first protein selected from the group consisting of:

(i) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a

nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,

(ii) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,

(iii) "Pen-2" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions, and

(iv) "Presenilin 1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions, and

(b) at least one second protein, which second protein is selected from the group consisting of:

(i) "Alpha-2 catenin" (SEQ ID No:280) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Alpha-2 catenin" encoded by a nucleic acid that hybridizes to the "Alpha-2 catenin" nucleic acid or its complement under low stringency conditions,

(ii) "COPINE FAMILY MEMBER" (SEQ ID No:281) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COPINE FAMILY MEMBER" encoded by a nucleic acid that hybridizes to the "COPINE FAMILY MEMBER" nucleic acid or its complement under low stringency conditions,

(iii) "Copine III" (SEQ ID No:282) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Copine III" encoded by a nucleic acid that hybridizes to the "Copine III" nucleic acid or its complement under low stringency conditions,

(iv) "Dachshund 2" (SEQ ID No:283) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dachshund 2" encoded by a nucleic acid that hybridizes to the "Dachshund 2" nucleic acid or its complement under low stringency conditions,

(v) "Delta-1 catenin" (SEQ ID No:284) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-1

catenin" encoded by a nucleic acid that hybridizes to the "Delta-1 catenin" nucleic acid or its complement under low stringency conditions,

(vi) "KIAA1102 (Fragment)" (SEQ ID No:285) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions,

(vii) "MGC2803" (SEQ ID No:286) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC2803" encoded by a nucleic acid that hybridizes to the "MGC2803" nucleic acid or its complement under low stringency conditions,

(viii) "Presenilin 2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions,

(ix) "TNRC15" (SEQ ID No:287) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TNRC15" encoded by a nucleic acid that hybridizes to the "TNRC15" nucleic acid or its complement under low stringency conditions,

(x) "TPST1" (SEQ ID No:288) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TPST1" encoded by a nucleic acid that hybridizes to the "TPST1" nucleic acid or its complement under low stringency conditions, and

(xi) "ZIP kinase" (SEQ ID No:289) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ZIP kinase" encoded by a nucleic acid that hybridizes to the "ZIP kinase" nucleic acid or its complement under low stringency conditions, and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

2. The protein complex according to No. 1 wherein the first protein is the protein 'Pen-2' (SEQ ID NO. 209), or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of 'Pen-2' encoded by a nucleic acid that hybridizes to the 'Pen-2' under low stringency conditions.
  
3. The protein complex according to No. 1 selected from complex (I) and comprising the following proteins:
  - (i) "Alpha-2 catenin" (SEQ ID No:280) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Alpha-2 catenin" encoded by a nucleic acid that hybridizes to the "Alpha-2 catenin" nucleic acid or its complement under low stringency conditions,
  - (ii) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,
  - (iii) "COPINE FAMILY MEMBER" (SEQ ID No:281) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COPINE FAMILY MEMBER" encoded by a nucleic acid that hybridizes to the "COPINE FAMILY MEMBER" nucleic acid or its complement under low stringency conditions,
  - (iv) "Copine III" (SEQ ID No:282) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Copine III" encoded by a nucleic acid that hybridizes to the "Copine III" nucleic acid or its complement under low stringency conditions,
  - (v) "Dachshund 2" (SEQ ID No:283) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dachshund 2" encoded by a nucleic acid that hybridizes to the "Dachshund 2" nucleic acid or its complement under low stringency conditions,
  - (vi) "Delta-1 catenin" (SEQ ID No:284) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-1 catenin" encoded by a nucleic acid that hybridizes to the "Delta-1 catenin" nucleic acid or its complement under low stringency conditions,
  - (vii) "KIAA1102 (Fragment)" (SEQ ID No:285) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102

(Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions,

(viii) "MGC2803" (SEQ ID No:286) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC2803" encoded by a nucleic acid that hybridizes to the "MGC2803" nucleic acid or its complement under low stringency conditions,

(ix) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,

(x) "Pen-2" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions,

(xi) "Presenilin 1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions,

(xii) "Presenilin 2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions,

(xiii) "TNRC15" (SEQ ID No:287) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TNRC15" encoded by a nucleic acid that hybridizes to the "TNRC15" nucleic acid or its complement under low stringency conditions,

(xiv) "TPST1" (SEQ ID No:288) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TPST1" encoded by a nucleic acid that hybridizes to the "TPST1" nucleic acid or its complement under low stringency conditions, and/or

(xv) "ZIP kinase" (SEQ ID No:289) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ZIP kinase" encoded by a nucleic acid that hybridizes to the "ZIP kinase" nucleic acid or its complement under low stringency conditions,

and a protein complex selected from complex (II) and comprising the following proteins:

- (i) "Alpha-2 catenin" (SEQ ID No:280) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Alpha-2 catenin" encoded by a nucleic acid that hybridizes to the "Alpha-2 catenin" nucleic acid or its complement under low stringency conditions,
- (ii) "COPINE FAMILY MEMBER" (SEQ ID No:281) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COPINE FAMILY MEMBER" encoded by a nucleic acid that hybridizes to the "COPINE FAMILY MEMBER" nucleic acid or its complement under low stringency conditions,
- (iii) "Copine III" (SEQ ID No:282) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Copine III" encoded by a nucleic acid that hybridizes to the "Copine III" nucleic acid or its complement under low stringency conditions,
- (iv) "Dachshund 2" (SEQ ID No:283) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dachshund 2" encoded by a nucleic acid that hybridizes to the "Dachshund 2" nucleic acid or its complement under low stringency conditions,
- (v) "Delta-1 catenin" (SEQ ID No:284) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-1 catenin" encoded by a nucleic acid that hybridizes to the "Delta-1 catenin" nucleic acid or its complement under low stringency conditions,
- (vi) "KIAA1102 (Fragment)" (SEQ ID No:285) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions,
- (vii) "MGC2803" (SEQ ID No:286) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC2803" encoded by a nucleic acid that hybridizes to the "MGC2803" nucleic acid or its complement under low stringency conditions,
- (viii) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,

- (ix) "Pen-2" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions,
- (x) "Presenilin 1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions,
- (xi) "Presenilin 2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions,
- (xii) "TNRC15" (SEQ ID No:287) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TNRC15" encoded by a nucleic acid that hybridizes to the "TNRC15" nucleic acid or its complement under low stringency conditions,
- (xiii) "TPST1" (SEQ ID No:288) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TPST1" encoded by a nucleic acid that hybridizes to the "TPST1" nucleic acid or its complement under low stringency conditions, and/or
- (xiv) "ZIP kinase" (SEQ ID No:289) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ZIP kinase" encoded by a nucleic acid that hybridizes to the "ZIP kinase" nucleic acid or its complement under low stringency conditions.

4. The protein complex according to No. 1 comprising all but 1 - 10 of the following proteins:

- (i) "Alpha-2 catenin" (SEQ ID No:280) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Alpha-2 catenin" encoded by a nucleic acid that hybridizes to the "Alpha-2 catenin" nucleic acid or its complement under low stringency conditions,
- (ii) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a



nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,

(iii) "COPINE FAMILY MEMBER" (SEQ ID No:281) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COPINE FAMILY MEMBER" encoded by a nucleic acid that hybridizes to the "COPINE FAMILY MEMBER" nucleic acid or its complement under low stringency conditions,

(iv) "Copine III" (SEQ ID No:282) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Copine III" encoded by a nucleic acid that hybridizes to the "Copine III" nucleic acid or its complement under low stringency conditions,

(v) "Dachshund 2" (SEQ ID No:283) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dachshund 2" encoded by a nucleic acid that hybridizes to the "Dachshund 2" nucleic acid or its complement under low stringency conditions,

(vi) "Delta-1 catenin" (SEQ ID No:284) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-1 catenin" encoded by a nucleic acid that hybridizes to the "Delta-1 catenin" nucleic acid or its complement under low stringency conditions,

(vii) "KIAA1102 (Fragment)" (SEQ ID No:285) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions,

(viii) "MGC2803" (SEQ ID No:286) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC2803" encoded by a nucleic acid that hybridizes to the "MGC2803" nucleic acid or its complement under low stringency conditions,

(ix) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,

(x) "Pen-2" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions,

- (xi) "Presenilin 1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions,
- (xii) "Presenilin 2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions,
- (xiii) "TNRC15" (SEQ ID No:287) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TNRC15" encoded by a nucleic acid that hybridizes to the "TNRC15" nucleic acid or its complement under low stringency conditions,
- (xiv) "TPST1" (SEQ ID No:288) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TPST1" encoded by a nucleic acid that hybridizes to the "TPST1" nucleic acid or its complement under low stringency conditions,
- (xv) "ZIP kinase" (SEQ ID No:289) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ZIP kinase" encoded by a nucleic acid that hybridizes to the "ZIP kinase" nucleic acid or its complement under low stringency conditions.

5. The complex of any of No. 1 - 4 comprising a functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein, respectively.

6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.

7. The complex of any of No. 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.

8. The complex of any of No. 1 - 7 that is involved in the the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)).

9. A process for preparing a complex of any of No. 1 - 8 and optionally the components thereof comprising the following steps: expressing a protein (bait) of the complex, preferably a tagged protein, in a target cell, isolating the protein complex which is attached to the bait protein, and optionally dissociating the protein complex and isolating the individual complex members.

10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.

11. The process according to any of No. 9 - 10 wherein the two tags are separated by a cleavage site for a protease.

12. Component of the Pen-2 complex obtainable by a process according to any of No. 9 - 11.

13. Protein of the Pen-2 complex selected from

(i) "COPINE FAMILY MEMBER" (SEQ ID No:281) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"COPINE FAMILY MEMBER" encoded by a nucleic acid that hybridizes to the "COPINE FAMILY MEMBER" nucleic acid or its complement under low stringency conditions,

(ii) "KIAA1102 (Fragment)" (SEQ ID No:285) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions,

(iii) "MGC2803" (SEQ ID No:286) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC2803" encoded by a nucleic acid that hybridizes to the "MGC2803" nucleic acid or its complement under low stringency conditions, and

(iv) "TNRC15" (SEQ ID No:287) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TNRC15" encoded by a nucleic acid that hybridizes to the "TNRC15" nucleic acid or its complement under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

14. Nucleic acid encoding a protein according to No. 13.

15. Construct, preferably a vector construct, comprising (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or

(b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative of at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the second group of proteins according to No. 1 (b).

16. Host cell, containing a vector comprising at least one of the nucleic acid of No. 14 and/or a construct of No. 15 or containing several vectors each comprising at least the nucleic acid sequence encoding at least one of the proteins, or functionally active fragments or functionally active derivatives thereof selected from the first group of proteins according to No. 1 (a) and the proteins, or functionally active fragments or functionally active derivatives thereof selected from the second group of proteins according to No. 1 (b).

17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody which binds to any of the proteins according to No. 13.

18. A kit comprising in one or more container the complex of any of No. 1 - 8 and/or the proteins of No. 13 optionally together with an antibody according to No. 17 and/or further components such as reagents and working instructions.

19. The kit according to No. 18 for processing a substrate of said complex.

20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

21. Array, in which at least a complex according to any of No. 1 - 8 and/or at least one protein according to No. 14 and/or at least one antibody according to No. 17 is attached to a solid carrier.

22. A process for processing a physiological substrate of the complex comprising the step of bringing into contact a complex to any of No. 1 - 8 with said substrate, such that said substrate is processed.

23. A pharmaceutical composition comprising the protein complex of any of No. 1 - 8 and/or any of the following the proteins:

- (i) "COPINE FAMILY MEMBER" (SEQ ID No:281) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COPINE FAMILY MEMBER" encoded by a nucleic acid that hybridizes to the "COPINE FAMILY MEMBER" nucleic acid or its complement under low stringency conditions,
- (ii) "KIAA1102 (Fragment)" (SEQ ID No:285) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions,
- (iii) "MGC2803" (SEQ ID No:286) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC2803" encoded by a nucleic acid that hybridizes to the "MGC2803" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "TNRC15" (SEQ ID No:287) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TNRC15" encoded by a nucleic acid that hybridizes to the "TNRC15" nucleic acid or its complement under low stringency conditions, and a pharmaceutical acceptable carrier.

24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

25. A method for screening for a molecule that binds to the complex of anyone of No. 1 - 8 and/or any of the following the proteins:

- (i) "COPINE FAMILY MEMBER" (SEQ ID No:281) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COPINE FAMILY MEMBER" encoded by a nucleic acid that hybridizes to the "COPINE FAMILY MEMBER" nucleic acid or its complement under low stringency conditions,
- (ii) "KIAA1102 (Fragment)" (SEQ ID No:285) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions,

(iii) "MGC2803" (SEQ ID No:286) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC2803" encoded by a nucleic acid that hybridizes to the "MGC2803" nucleic acid or its complement under low stringency conditions, and/or

(iv) "TNRC15" (SEQ ID No:287) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TNRC15" encoded by a nucleic acid that hybridizes to the "TNRC15" nucleic acid or its complement under low stringency conditions, comprising the steps of

(a) exposing said complex, or a cell or organism containing same to one or more candidate molecules; and

(b) determining whether said candidate molecule is bound to the complex or protein.

26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 - 8 comprising the steps of (a) exposing said complex, or a cell or organism containing Pen-2 complex to one or more candidate molecules; and

(b) determining the amount of activity of protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.

27. The method of No. 26, wherein the amount of said complex is determined.

28. The method of No. 26, wherein the activity of said complex is determined.

29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining the processing of said substrate is modified in the presence of said candidate molecule.

30. The method of No. 26, wherein the amount of the individual protein components of said complex are determined.

31. The method of No. 30, wherein said determining step comprises determining whether

(i) "Alpha-2 catenin" (SEQ ID No:280) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Alpha-2 catenin" encoded by a nucleic acid that hybridizes to the "Alpha-2 catenin" nucleic acid or its complement under low stringency conditions, and/or

(ii) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions, and/or

(iii) "COPINE FAMILY MEMBER" (SEQ ID No:281) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COPINE FAMILY MEMBER" encoded by a nucleic acid that hybridizes to the "COPINE FAMILY MEMBER" nucleic acid or its complement under low stringency conditions, and/or

(iv) "Copine III" (SEQ ID No:282) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Copine III" encoded by a nucleic acid that hybridizes to the "Copine III" nucleic acid or its complement under low stringency conditions, and/or

(v) "Dachshund 2" (SEQ ID No:283) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dachshund 2" encoded by a nucleic acid that hybridizes to the "Dachshund 2" nucleic acid or its complement under low stringency conditions, and/or

(vi) "Delta-1 catenin" (SEQ ID No:284) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-1



catenin" encoded by a nucleic acid that hybridizes to the "Delta-1 catenin" nucleic acid or its complement under low stringency conditions, and/or

(vii) "KIAA1102 (Fragment)" (SEQ ID No:285) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions, and/or

(viii) "MGC2803" (SEQ ID No:286) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC2803" encoded by a nucleic acid that hybridizes to the "MGC2803" nucleic acid or its complement under low stringency conditions, and/or

(ix) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions, and/or

(x) "Pen-2" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions, and/or

(xi) "Presenilin 1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions, and/or

(xii) "Presenilin 2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions, and/or

(xiii) "TNRC15" (SEQ ID No:287) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TNRC15" encoded by a nucleic acid that hybridizes to the "TNRC15" nucleic acid or its complement under low stringency conditions, and/or

(xiv) "TPST1" (SEQ ID No:288) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TPST1" encoded by a nucleic acid that hybridizes to the "TPST1" nucleic acid or its complement under low stringency conditions, and/or

(xv) "ZIP kinase" (SEQ ID No:289) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ZIP kinase" encoded by a nucleic acid that hybridizes to the "ZIP kinase" nucleic acid or its complement under low stringency conditions, is present in the complex.

32. The method of any of No. 26 - 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 - 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

34. A method for the production of a pharmaceutical composition comprising carrying out the method of any of No. 1 - 8 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.

35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, activity of, or component composition of, or intracellular localization of the complex of any one of the No. 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in an analogous sample from a subject not having the disease or disorder or predisposition indicates the presence in the subject of the disease or disorder or predisposition in the subject.

36. The method of No. 35, wherein the amount of said complex is determined.

37. The method of No. 35, wherein the activity of said complex is determined.

38. The method of No. 37, wherein said determining step comprises isolating from the subject said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.

39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.

40. The method of No. 39, wherein said determining step comprises determining whether (i) "Alpha-2 catenin" (SEQ ID No:280) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Alpha-2 catenin" encoded by a nucleic acid that hybridizes to the "Alpha-2 catenin" nucleic acid or its complement under low stringency conditions, and/or

(ii) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions, and/or

(iii) "COPINE FAMILY MEMBER" (SEQ ID No:281) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COPINE FAMILY MEMBER" encoded by a nucleic acid that hybridizes to the "COPINE FAMILY MEMBER" nucleic acid or its complement under low stringency conditions, and/or

(iv) "Copine III" (SEQ ID No:282) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Copine III" encoded by a nucleic acid that hybridizes to the "Copine III" nucleic acid or its complement under low stringency conditions, and/or

(v) "Dachshund 2" (SEQ ID No:283) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dachshund 2" encoded by a nucleic acid that hybridizes to the "Dachshund 2" nucleic acid or its complement under low stringency conditions, and/or

- (vi) "Delta-1 catenin" (SEQ ID No:284) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-1 catenin" encoded by a nucleic acid that hybridizes to the "Delta-1 catenin" nucleic acid or its complement under low stringency conditions, and/or
- (vii) "KIAA1102 (Fragment)" (SEQ ID No:285) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions, and/or
- (viii) "MGC2803" (SEQ ID No:286) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC2803" encoded by a nucleic acid that hybridizes to the "MGC2803" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions, and/or
- (x) "Pen-2" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "Presenilin 1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions, and/or
- (xii) "Presenilin 2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions, and/or
- (xiii) "TNRC15" (SEQ ID No:287) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TNRC15" encoded by a nucleic acid that hybridizes to the "TNRC15" nucleic acid or its complement under low stringency conditions, and/or
- (xiv) "TPST1" (SEQ ID No:288) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TPST1"

encoded by a nucleic acid that hybridizes to the "TPST1" nucleic acid or its complement under low stringency conditions, and/or

(xv) "ZIP kinase" (SEQ ID No:289) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ZIP kinase" encoded by a nucleic acid that hybridizes to the "ZIP kinase" nucleic acid or its complement under low stringency conditions, is present in the complex.

41. The complex of any one of No. 1 - 8, or proteins of No. 13 or the antibody or fragment of No. 17, for use in a method of diagnosing a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity or component composition of or intracellular localization of, the complex of anyone of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), or protein components of, said complex.

43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.

44. The method according to No. 42 , wherein said disease or disorder involves increased levels of the amount or activity of said complex.

45. Complex of any of No. 1 - 8 and/or protein selected from the following proteins

- (i) "Alpha-2 catenin" (SEQ ID No:280) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Alpha-2 catenin" encoded by a nucleic acid that hybridizes to the "Alpha-2 catenin" nucleic acid or its complement under low stringency conditions,
- (ii) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,
- (iii) "COPINE FAMILY MEMBER" (SEQ ID No:281) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COPINE FAMILY MEMBER" encoded by a nucleic acid that hybridizes to the "COPINE FAMILY MEMBER" nucleic acid or its complement under low stringency conditions,
- (iv) "Copine III" (SEQ ID No:282) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Copine III" encoded by a nucleic acid that hybridizes to the "Copine III" nucleic acid or its complement under low stringency conditions,
- (v) "Dachshund 2" (SEQ ID No:283) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dachshund 2" encoded by a nucleic acid that hybridizes to the "Dachshund 2" nucleic acid or its complement under low stringency conditions,
- (vi) "Delta-1 catenin" (SEQ ID No:284) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-1 catenin" encoded by a nucleic acid that hybridizes to the "Delta-1 catenin" nucleic acid or its complement under low stringency conditions,
- (vii) "KIAA1102 (Fragment)" (SEQ ID No:285) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions,
- (viii) "MGC2803" (SEQ ID No:286) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC2803"

encoded by a nucleic acid that hybridizes to the "MGC2803" nucleic acid or its complement under low stringency conditions,

(ix) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,

(x) "Pen-2" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions,

(xi) "Presenilin 1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions,

(xii) "Presenilin 2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions,

(xiii) "TNRC15" (SEQ ID No:287) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TNRC15" encoded by a nucleic acid that hybridizes to the "TNRC15" nucleic acid or its complement under low stringency conditions,

(xiv) "TPST1" (SEQ ID No:288) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TPST1" encoded by a nucleic acid that hybridizes to the "TPST1" nucleic acid or its complement under low stringency conditions, and/or (xv) "ZIP kinase" (SEQ ID No:289) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ZIP kinase" encoded by a nucleic acid that hybridizes to the "ZIP kinase" nucleic acid or its complement under low stringency conditions, as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

The present invention further relates to the following embodiments of the APP695SW-complex

1. A protein complex selected from complex (I) and comprising
  - (a) at least one first protein selected from the group consisting of:
    - (i) "APP695SW" (SEQ ID No:290) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP695SW" encoded by a nucleic acid that hybridizes to the "APP695SW" nucleic acid or its complement under low stringency conditions,
    - (ii) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,
    - (iii) "Fe65L1" (SEQ ID No:292) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions,
    - (iv) "JIP-1" (SEQ ID No:295) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "JIP-1" encoded by a nucleic acid that hybridizes to the "JIP-1" nucleic acid or its complement under low stringency conditions, and
    - (v) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions, and
  - (b) at least one second protein, which second protein is selected from the group consisting of:
    - (i) "FLJ10773" (SEQ ID No:291) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ10773" encoded by a nucleic acid that hybridizes to the "FLJ10773" nucleic acid or its complement under low stringency conditions,
    - (ii) "GTF2I" (SEQ ID No:293) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GTF2I" encoded by a



nucleic acid that hybridizes to the "GTF2I" nucleic acid or its complement under low stringency conditions,

(iii) "IL13RA2" (SEQ ID No:294) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IL13RA2" encoded by a nucleic acid that hybridizes to the "IL13RA2" nucleic acid or its complement under low stringency conditions,

(iv) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions,

(v) "Integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "Integral membrane transporter protein" nucleic acid or its complement under low stringency conditions, and

(vi) "S-100 alpha" (SEQ ID No:296) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions, and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

2. The protein complex according to No. 1 wherein the first protein is the protein 'APP695SW' (SEQ ID NO. 290), or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of 'APP695SW' encoded by a nucleic acid that hybridizes to the 'APP695SW' under low stringency conditions.

3. The protein complex according to No. 1 selected from complex (I) and comprising the following proteins:

- (i) "APP695SW" (SEQ ID No:290) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP695SW" encoded by a nucleic acid that hybridizes to the "APP695SW" nucleic acid or its complement under low stringency conditions,
- (ii) "FLJ10773" (SEQ ID No:291) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ10773" encoded by a nucleic acid that hybridizes to the "FLJ10773" nucleic acid or its complement under low stringency conditions,
- (iii) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,
- (iv) "Fe65L1" (SEQ ID No:292) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions,
- (v) "GTF2I" (SEQ ID No:293) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GTF2I" encoded by a nucleic acid that hybridizes to the "GTF2I" nucleic acid or its complement under low stringency conditions,
- (vi) "IL13RA2" (SEQ ID No:294) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IL13RA2" encoded by a nucleic acid that hybridizes to the "IL13RA2" nucleic acid or its complement under low stringency conditions,
- (vii) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions,
- (viii) "Integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane transporter protein" encoded by a nucleic acid that

hybridizes to the "Integral membrane transporter protein" nucleic acid or its complement under low stringency conditions,

(ix) "JIP-1" (SEQ ID No:295) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "JIP-1" encoded by a nucleic acid that hybridizes to the "JIP-1" nucleic acid or its complement under low stringency conditions,

(x) "S-100 alpha" (SEQ ID No:296) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions, and/or

(xi) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions,

and a protein complex selected from complex (II) and comprising the following proteins:

(i) "APP695SW" (SEQ ID No:290) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP695SW" encoded by a nucleic acid that hybridizes to the "APP695SW" nucleic acid or its complement under low stringency conditions,

(ii) "FLJ10773" (SEQ ID No:291) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ10773" encoded by a nucleic acid that hybridizes to the "FLJ10773" nucleic acid or its complement under low stringency conditions,

(iii) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,

(iv) "Fe65L1" (SEQ ID No:292) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions,

(v) "GTF2I" (SEQ ID No:293) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GTF2I" encoded by a

nucleic acid that hybridizes to the "GTF2I" nucleic acid or its complement under low stringency conditions,

(vi) "IL13RA2" (SEQ ID No:294) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IL13RA2" encoded by a nucleic acid that hybridizes to the "IL13RA2" nucleic acid or its complement under low stringency conditions,

(vii) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions,

(viii) "Integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "Integral membrane transporter protein" nucleic acid or its complement under low stringency conditions,

(ix) "S-100 alpha" (SEQ ID No:296) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions, and/or

(x) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions.

4. The protein complex according to No. 1 comprising all but 1 - 5 of the following proteins:

(i) "APP695SW" (SEQ ID No:290) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP695SW" encoded by a nucleic acid that hybridizes to the "APP695SW" nucleic acid or its complement under low stringency conditions,

(ii) "FLJ10773" (SEQ ID No:291) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ10773"

encoded by a nucleic acid that hybridizes to the "FLJ10773" nucleic acid or its complement under low stringency conditions,

(iii) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,

(iv) "Fe65L1" (SEQ ID No:292) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions,

(v) "GTF2I" (SEQ ID No:293) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GTF2I" encoded by a nucleic acid that hybridizes to the "GTF2I" nucleic acid or its complement under low stringency conditions,

(vi) "IL13RA2" (SEQ ID No:294) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IL13RA2" encoded by a nucleic acid that hybridizes to the "IL13RA2" nucleic acid or its complement under low stringency conditions,

(vii) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions,

(viii) "Integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "Integral membrane transporter protein" nucleic acid or its complement under low stringency conditions,

(ix) "JIP-1" (SEQ ID No:295) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "JIP-1" encoded by a nucleic acid that hybridizes to the "JIP-1" nucleic acid or its complement under low stringency conditions,

(x) "S-100 alpha" (SEQ ID No:296) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 alpha"

encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions,

(xi) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions.

5. The complex of any of No. 1 - 4 comprising a functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein, respectively.

6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.

7. The complex of any of No. 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.

8. The complex of any of No. 1 - 7 that is involved in the the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)).

9. A process for preparing a complex of any of No. 1 - 8 and optionally the components thereof comprising the following steps: expressing a protein (bait) of the complex, preferably a tagged protein, in a target cell, isolating the protein complex which is attached to the bait protein, and optionally dissociating the protein complex and isolating the individual complex members.

10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.

11. The process according to any of No. 9 - 10 wherein the two tags are separated by a cleavage site for a protease.

12. Component of the APP695SW complex obtainable by a process according to any of No. 9 - 11.

13. Protein of the APP695SW complex selected from

(i) "FLJ10773" (SEQ ID No:291) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ10773" encoded by a nucleic acid that hybridizes to the "FLJ10773" nucleic acid or its complement under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

14. Nucleic acid encoding a protein according to No. 13.

15. Construct, preferably a vector construct, comprising (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or

(b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative of at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the second group of proteins according to No. 1 (b).

16. Host cell, containing a vector comprising at least one of the nucleic acid of No. 14 and/or a construct of No. 15 or containing several vectors each comprising at least the nucleic acid sequence encoding at least one of the proteins, or functionally active fragments or functionally active derivatives thereof selected from the first group of proteins according to No. 1 (a) and the proteins, or functionally active fragments or functionally active derivatives thereof selected from the second group of proteins according to No. 1 (b).

17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody which binds to any of the proteins according to No. 13.

18. A kit comprising in one or more container the complex of any of No. 1 - 8 and/or the proteins of No. 13 optionally together with an antibody according to No. 17 and/or further components such as reagents and working instructions.

19. The kit according to No. 18 for processing a substrate of said complex.

20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.



21. Array, in which at least a complex according to any of No. 1 - 8 and/or at least one protein according to No. 14 and/or at least one antibody according to No. 17 is attached to a solid carrier.

22. A process for processing a physiological substrate of the complex comprising the step of bringing into contact a complex to any of No. 1 - 8 with said substrate, such that said substrate is processed.

23. A pharmaceutical composition comprising the protein complex of any of No. 1 - 8 and/or any of the following the proteins:

(i) "FLJ10773" (SEQ ID No:291) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ10773" encoded by a nucleic acid that hybridizes to the "FLJ10773" nucleic acid or its complement under low stringency conditions, and a pharmaceutical acceptable carrier.

24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

25. A method for screening for a molecule that binds to the complex of anyone of No. 1 - 8 and/or any of the following the proteins:

(i) "FLJ10773" (SEQ ID No:291) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ10773" encoded by a nucleic acid that hybridizes to the "FLJ10773" nucleic acid or its complement under low stringency conditions, comprising the steps of

(a) exposing said complex, or a cell or organism containing same to one or more candidate molecules; and

(b) determining whether said candidate molecule is bound to the complex or protein.

26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 - 8

comprising the steps of (a) exposing said complex, or a cell or organism containing APP695SW complex to one or more candidate molecules; and

(b) determining the amount of activity of protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.

27. The method of No. 26, wherein the amount of said complex is determined.

28. The method of No. 26, wherein the activity of said complex is determined.

29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining the processing of said substrate is modified in the presence of said candidate molecule.

30. The method of No. 26, wherein the amount of the individual protein components of said complex are determined.

31. The method of No. 30, wherein said determining step comprises determining whether (i) "APP695SW" (SEQ ID No:290) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP695SW" encoded by a nucleic acid that hybridizes to the "APP695SW" nucleic acid or its complement under low stringency conditions, and/or

- (ii) "FLJ10773" (SEQ ID No:291) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ10773" encoded by a nucleic acid that hybridizes to the "FLJ10773" nucleic acid or its complement under low stringency conditions, and/or
- (iii) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "Fe65L1" (SEQ ID No:292) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions, and/or
- (v) "GTF2I" (SEQ ID No:293) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GTF2I" encoded by a nucleic acid that hybridizes to the "GTF2I" nucleic acid or its complement under low stringency conditions, and/or
- (vi) "IL13RA2" (SEQ ID No:294) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IL13RA2" encoded by a nucleic acid that hybridizes to the "IL13RA2" nucleic acid or its complement under low stringency conditions, and/or
- (vii) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions, and/or
- (viii) "Integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "Integral membrane transporter protein" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "JIP-1" (SEQ ID No:295) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "JIP-1" encoded by a nucleic acid that hybridizes to the "JIP-1" nucleic acid or its complement under low stringency conditions, and/or

(x) "S-100 alpha" (SEQ ID No:296) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions, and/or

(xi) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions, is present in the complex.

32. The method of any of No. 26 - 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 - 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

34. A method for the production of a pharmaceutical composition comprising carrying out the method of any of No. 1 - 8 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.

35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, activity of, or component composition of, or intracellular localization of the complex of any one of the No. 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in an analogous sample from a subject not

having the disease or disorder or predisposition indicates the presence in the subject of the disease or disorder or predisposition in the subject.

36. The method of No. 35, wherein the amount of said complex is determined.

37. The method of No. 35, wherein the activity of said complex is determined.

38. The method of No. 37, wherein said determining step comprises isolating from the subject said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.

39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.

40. The method of No. 39, wherein said determining step comprises determining whether (i) "APP695SW" (SEQ ID No:290) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP695SW" encoded by a nucleic acid that hybridizes to the "APP695SW" nucleic acid or its complement under low stringency conditions, and/or

(ii) "FLJ10773" (SEQ ID No:291) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ10773" encoded by a nucleic acid that hybridizes to the "FLJ10773" nucleic acid or its complement under low stringency conditions, and/or

(iii) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions, and/or

(iv) "Fe65L1" (SEQ ID No:292) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions, and/or

- (v) "GTF2I" (SEQ ID No:293) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GTF2I" encoded by a nucleic acid that hybridizes to the "GTF2I" nucleic acid or its complement under low stringency conditions, and/or
- (vi) "IL13RA2" (SEQ ID No:294) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IL13RA2" encoded by a nucleic acid that hybridizes to the "IL13RA2" nucleic acid or its complement under low stringency conditions, and/or
- (vii) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions, and/or
- (viii) "Integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "Integral membrane transporter protein" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "JIP-1" (SEQ ID No:295) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "JIP-1" encoded by a nucleic acid that hybridizes to the "JIP-1" nucleic acid or its complement under low stringency conditions, and/or
- (x) "S-100 alpha" (SEQ ID No:296) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions, is present in the complex.

41. The complex of any one of No. 1 - 8, or proteins of No. 13 or the antibody or fragment of No. 17, for use in a method of diagnosing a disease or disorder such as

neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity or component composition of or intracellular localization of, the complex of anyone of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), or protein components of, said complex.

43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.

44. The method according to No. 42, wherein said disease or disorder involves increased levels of the amount or activity of said complex.

45. Complex of any of No. 1 - 8 and/or protein selected from the following proteins

(i) "APP695SW" (SEQ ID No:290) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP695SW" encoded by a nucleic acid that hybridizes to the "APP695SW" nucleic acid or its complement under low stringency conditions,

(ii) "FLJ10773" (SEQ ID No:291) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ10773"

encoded by a nucleic acid that hybridizes to the "FLJ10773" nucleic acid or its complement under low stringency conditions,

(iii) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,

(iv) "Fe65L1" (SEQ ID No:292) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions,

(v) "GTF2I" (SEQ ID No:293) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GTF2I" encoded by a nucleic acid that hybridizes to the "GTF2I" nucleic acid or its complement under low stringency conditions,

(vi) "IL13RA2" (SEQ ID No:294) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IL13RA2" encoded by a nucleic acid that hybridizes to the "IL13RA2" nucleic acid or its complement under low stringency conditions,

(vii) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions,

(viii) "Integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "Integral membrane transporter protein" nucleic acid or its complement under low stringency conditions,

(ix) "JIP-1" (SEQ ID No:295) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "JIP-1" encoded by a nucleic acid that hybridizes to the "JIP-1" nucleic acid or its complement under low stringency conditions,

(x) "S-100 alpha" (SEQ ID No:296) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 alpha"



encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions, and/or(xi) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions, as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

The present invention further relates to the following embodiments of the APP-C99-complex

1. A protein complex selected from complex (I) and comprising
  - (a) at least one first protein selected from the group consisting of:
    - (i) "APP-C99" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP-C99" encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid or its complement under low stringency conditions,
    - (ii) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,
    - (iii) "Fe65L1" (SEQ ID No:292) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions, and
    - (iv) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions, and
  - (b) at least one second protein, which second protein is selected from the group consisting of:
    - (i) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid

that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,

(ii) "CAMK2D" (SEQ ID No:297) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CAMK2D" encoded by a nucleic acid that hybridizes to the "CAMK2D" nucleic acid or its complement under low stringency conditions,

(iii) "Delta-like homolog" (SEQ ID No:298) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-like homolog" encoded by a nucleic acid that hybridizes to the "Delta-like homolog" nucleic acid or its complement under low stringency conditions,

(iv) "Integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "Integral membrane transporter protein" nucleic acid or its complement under low stringency conditions,

(v) "KIAA1102 (Fragment)" (SEQ ID No:285) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions,

(vi) "KIAA1949" (SEQ ID No:299) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1949" encoded by a nucleic acid that hybridizes to the "KIAA1949" nucleic acid or its complement under low stringency conditions,

(vii) "MGC4022" (SEQ ID No:300) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4022" encoded by a nucleic acid that hybridizes to the "MGC4022" nucleic acid or its complement under low stringency conditions,

(viii) "MGC5442" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions,

(ix) "NAP-1 related protein" (SEQ ID No:301) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NAP-1

related protein" encoded by a nucleic acid that hybridizes to the "NAP-1 related protein" nucleic acid or its complement under low stringency conditions,

(x) "Neurocalcin delta" (SEQ ID No:302) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurocalcin delta" encoded by a nucleic acid that hybridizes to the "Neurocalcin delta" nucleic acid or its complement under low stringency conditions,

(xi) "REST corepressor" (SEQ ID No:303) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "REST corepressor" encoded by a nucleic acid that hybridizes to the "REST corepressor" nucleic acid or its complement under low stringency conditions,

(xii) "S-100 alpha" (SEQ ID No:296) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions, and

(xiii) "S-100 beta" (SEQ ID No:304) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 beta" encoded by a nucleic acid that hybridizes to the "S-100 beta" nucleic acid or its complement under low stringency conditions, and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

2. The protein complex according to No. 1 wherein the first protein is the protein APP-C99 (SEQ ID NO. 10), or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of 'APP-C99' encoded by a nucleic acid that hybridizes to the 'APP-C99' under low stringency conditions.

3. The protein complex according to No. 1 selected from complex (I) and comprising the following proteins:

- (i) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
- (ii) "APP-C99" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP-C99" encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid or its complement under low stringency conditions,
- (iii) "CAMK2D" (SEQ ID No:297) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CAMK2D" encoded by a nucleic acid that hybridizes to the "CAMK2D" nucleic acid or its complement under low stringency conditions,
- (iv) "Delta-like homolog" (SEQ ID No:298) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-like homolog" encoded by a nucleic acid that hybridizes to the "Delta-like homolog" nucleic acid or its complement under low stringency conditions,
- (v) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,
- (vi) "Fe65L1" (SEQ ID No:292) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions,
- (vii) "Integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "Integral membrane transporter protein" nucleic acid or its complement under low stringency conditions,
- (viii) "KIAA1102 (Fragment)" (SEQ ID No:285) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions,

- (ix) "KIAA1949" (SEQ ID No:299) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1949" encoded by a nucleic acid that hybridizes to the "KIAA1949" nucleic acid or its complement under low stringency conditions,
- (x) "MGC4022" (SEQ ID No:300) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4022" encoded by a nucleic acid that hybridizes to the "MGC4022" nucleic acid or its complement under low stringency conditions,
- (xi) "MGC5442" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions,
- (xii) "NAP-1 related protein" (SEQ ID No:301) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NAP-1 related protein" encoded by a nucleic acid that hybridizes to the "NAP-1 related protein" nucleic acid or its complement under low stringency conditions,
- (xiii) "Neurocalcin delta" (SEQ ID No:302) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurocalcin delta" encoded by a nucleic acid that hybridizes to the "Neurocalcin delta" nucleic acid or its complement under low stringency conditions,
- (xiv) "REST corepressor" (SEQ ID No:303) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "REST corepressor" encoded by a nucleic acid that hybridizes to the "REST corepressor" nucleic acid or its complement under low stringency conditions,
- (xv) "S-100 alpha" (SEQ ID No:296) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions,
- (xvi) "S-100 beta" (SEQ ID No:304) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 beta" encoded by a nucleic acid that hybridizes to the "S-100 beta" nucleic acid or its complement under low stringency conditions, and/or
- (xvii) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta"

encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions,

and a protein complex selected from complex (II) and comprising the following proteins:

(i) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,

(ii) "APP-C99" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP-C99" encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid or its complement under low stringency conditions,

(iii) "CAMK2D" (SEQ ID No:297) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CAMK2D" encoded by a nucleic acid that hybridizes to the "CAMK2D" nucleic acid or its complement under low stringency conditions,

(iv) "Delta-like homolog" (SEQ ID No:298) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-like homolog" encoded by a nucleic acid that hybridizes to the "Delta-like homolog" nucleic acid or its complement under low stringency conditions,

(v) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,

(vi) "Fe65L1" (SEQ ID No:292) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions,

(vii) "Integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "Integral membrane transporter protein" nucleic acid or its complement under low stringency conditions,

(viii) "KIAA1102 (Fragment)" (SEQ ID No:285) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102

(Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions,

(ix) "KIAA1949" (SEQ ID No:299) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1949" encoded by a nucleic acid that hybridizes to the "KIAA1949" nucleic acid or its complement under low stringency conditions,

(x) "MGC4022" (SEQ ID No:300) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4022" encoded by a nucleic acid that hybridizes to the "MGC4022" nucleic acid or its complement under low stringency conditions,

(xi) "MGC5442" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions,

(xii) "NAP-1 related protein" (SEQ ID No:301) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NAP-1 related protein" encoded by a nucleic acid that hybridizes to the "NAP-1 related protein" nucleic acid or its complement under low stringency conditions,

(xiii) "Neurocalcin delta" (SEQ ID No:302) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurocalcin delta" encoded by a nucleic acid that hybridizes to the "Neurocalcin delta" nucleic acid or its complement under low stringency conditions,

(xiv) "REST corepressor" (SEQ ID No:303) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "REST corepressor" encoded by a nucleic acid that hybridizes to the "REST corepressor" nucleic acid or its complement under low stringency conditions,

(xv) "S-100 alpha" (SEQ ID No:296) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions,

(xvi) "S-100 beta" (SEQ ID No:304) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 beta" encoded by a nucleic acid that hybridizes to the "S-100 beta" nucleic acid or its complement under low stringency conditions, and/or

(xvii) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions.

4. The protein complex according to No. 1 comprising all but 1 - 12 of the following proteins:

(i) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,

(ii) "APP-C99" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP-C99" encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid or its complement under low stringency conditions,

(iii) "CAMK2D" (SEQ ID No:297) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CAMK2D" encoded by a nucleic acid that hybridizes to the "CAMK2D" nucleic acid or its complement under low stringency conditions,

(iv) "Delta-like homolog" (SEQ ID No:298) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-like homolog" encoded by a nucleic acid that hybridizes to the "Delta-like homolog" nucleic acid or its complement under low stringency conditions,

(v) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,

(vi) "Fe65L1" (SEQ ID No:292) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions,

(vii) "Integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane transporter protein" encoded by a nucleic acid that



hybridizes to the "Integral membrane transporter protein" nucleic acid or its complement under low stringency conditions,

(viii) "KIAA1102 (Fragment)" (SEQ ID No:285) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions,

(ix) "KIAA1949" (SEQ ID No:299) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1949" encoded by a nucleic acid that hybridizes to the "KIAA1949" nucleic acid or its complement under low stringency conditions,

(x) "MGC4022" (SEQ ID No:300) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4022" encoded by a nucleic acid that hybridizes to the "MGC4022" nucleic acid or its complement under low stringency conditions,

(xi) "MGC5442" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions,

(xii) "NAP-1 related protein" (SEQ ID No:301) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NAP-1 related protein" encoded by a nucleic acid that hybridizes to the "NAP-1 related protein" nucleic acid or its complement under low stringency conditions,

(xiii) "Neurocalcin delta" (SEQ ID No:302) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurocalcin delta" encoded by a nucleic acid that hybridizes to the "Neurocalcin delta" nucleic acid or its complement under low stringency conditions,

(xiv) "REST corepressor" (SEQ ID No:303) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "REST corepressor" encoded by a nucleic acid that hybridizes to the "REST corepressor" nucleic acid or its complement under low stringency conditions,

(xv) "S-100 alpha" (SEQ ID No:296) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions,

- (xvi) "S-100 beta" (SEQ ID No:304) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 beta" encoded by a nucleic acid that hybridizes to the "S-100 beta" nucleic acid or its complement under low stringency conditions,
- (xvii) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions.

5. The complex of any of No. 1 - 4 comprising a functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein, respectively.
6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.
7. The complex of any of No. 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.
8. The complex of any of No. 1 - 7 that is involved in the the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by

modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)).

9. A process for preparing a complex of any of No. 1 - 8 and optionally the components thereof comprising the following steps: expressing a protein (bait) of the complex, preferably a tagged protein, in a target cell, isolating the protein complex which is attached to the bait protein, and optionally dissociating the protein complex and isolating the individual complex members.

10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.

11. The process according to any of No. 9 - 10 wherein the two tags are separated by a cleavage site for a protease.

12. Component of the APP-C99 complex obtainable by a process according to any of No. 9 - 11.

13. Protein of the APP-C99 complex selected from

(i) "KIAA1102 (Fragment)" (SEQ ID No:285) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions,

(ii) "KIAA1949" (SEQ ID No:299) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1949" encoded by a nucleic acid that hybridizes to the "KIAA1949" nucleic acid or its complement under low stringency conditions,

(iii) "MGC4022" (SEQ ID No:300) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4022" encoded by a nucleic acid that hybridizes to the "MGC4022" nucleic acid or its complement under low stringency conditions, and

(iv) "MGC5442" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442"

encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

14. Nucleic acid encoding a protein according to No. 13.

15. Construct, preferably a vector construct, comprising (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or

(b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative of at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the second group of proteins according to No. 1 (b).

16. Host cell, containing a vector comprising at least one of the nucleic acid of No. 14 and/or a construct of No. 15 or containing several vectors each comprising at least the nucleic acid sequence encoding at least one of the proteins, or functionally active fragments or functionally active derivatives thereof selected from the first group of proteins according to No. 1 (a) and the proteins, or functionally active fragments or functionally active derivatives thereof selected from the second group of proteins according to No. 1 (b).

17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and

an antibody or a fragment of said antibody which binds to any of the proteins according to No. 13.

18. A kit comprising in one or more container the complex of any of No. 1 - 8 and/or the proteins of No. 13 optionally together with an antibody according to No. 17 and/or further components such as reagents and working instructions.

19. The kit according to No. 18 for processing a substrate of said complex.

20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

21. Array, in which at least a complex according to any of No. 1 - 8 and/or at least one protein according to No. 14 and/or at least one antibody according to No. 17 is attached to a solid carrier.

22. A process for processing a physiological substrate of the complex comprising the step of bringing into contact a complex to any of No. 1 - 8 with said substrate, such that said substrate is processed.

23. A pharmaceutical composition comprising the protein complex of any of No. 1 - 8 and/or any of the following the proteins:

- (i) "KIAA1102 (Fragment)" (SEQ ID No:285) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions,
- (ii) "KIAA1949" (SEQ ID No:299) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1949" encoded by a nucleic acid that hybridizes to the "KIAA1949" nucleic acid or its complement under low stringency conditions,
- (iii) "MGC4022" (SEQ ID No:300) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4022"

encoded by a nucleic acid that hybridizes to the "MGC4022" nucleic acid or its complement under low stringency conditions, and/or

(iv) "MGC5442" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions, and a pharmaceutical acceptable carrier.

24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

25. A method for screening for a molecule that binds to the complex of anyone of No. 1 - 8 and/or any of the following the proteins:

(i) "KIAA1102 (Fragment)" (SEQ ID No:285) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions,

(ii) "KIAA1949" (SEQ ID No:299) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1949" encoded by a nucleic acid that hybridizes to the "KIAA1949" nucleic acid or its complement under low stringency conditions,

(iii) "MGC4022" (SEQ ID No:300) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4022" encoded by a nucleic acid that hybridizes to the "MGC4022" nucleic acid or its complement under low stringency conditions, and/or

(iv) "MGC5442" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions, comprising the steps of

(a) exposing said complex, or a cell or organism containing same to one or more candidate molecules; and

(b) determining whether said candidate molecule is bound to the complex or protein.

26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 - 8 comprising the steps of (a) exposing said complex, or a cell or organism containing APP-C99 complex to one or more candidate molecules; and

(b) determining the amount of activity of protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.

27. The method of No. 26, wherein the amount of said complex is determined.

28. The method of No. 26, wherein the activity of said complex is determined.

29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining the processing of said substrate is modified in the presence of said candidate molecule.

30. The method of No. 26, wherein the amount of the individual protein components of said complex are determined.

31. The method of No. 30, wherein said determining step comprises determining whether (i) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid

that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions, and/or

(ii) "APP-C99" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP-C99" encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid or its complement under low stringency conditions, and/or

(iii) "CAMK2D" (SEQ ID No:297) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CAMK2D" encoded by a nucleic acid that hybridizes to the "CAMK2D" nucleic acid or its complement under low stringency conditions, and/or

(iv) "Delta-like homolog" (SEQ ID No:298) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-like homolog" encoded by a nucleic acid that hybridizes to the "Delta-like homolog" nucleic acid or its complement under low stringency conditions, and/or

(v) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions, and/or

(vi) "Fe65L1" (SEQ ID No:292) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions, and/or

(vii) "Integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "Integral membrane transporter protein" nucleic acid or its complement under low stringency conditions, and/or

(viii) "KIAA1102 (Fragment)" (SEQ ID No:285) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions, and/or

(ix) "KIAA1949" (SEQ ID No:299) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1949"



encoded by a nucleic acid that hybridizes to the "KIAA1949" nucleic acid or its complement under low stringency conditions, and/or

(x) "MGC4022" (SEQ ID No:300) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4022" encoded by a nucleic acid that hybridizes to the "MGC4022" nucleic acid or its complement under low stringency conditions, and/or

(xi) "MGC5442" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions, and/or

(xii) "NAP-1 related protein" (SEQ ID No:301) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NAP-1 related protein" encoded by a nucleic acid that hybridizes to the "NAP-1 related protein" nucleic acid or its complement under low stringency conditions, and/or

(xiii) "Neurocalcin delta" (SEQ ID No:302) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurocalcin delta" encoded by a nucleic acid that hybridizes to the "Neurocalcin delta" nucleic acid or its complement under low stringency conditions, and/or

(xiv) "REST corepressor" (SEQ ID No:303) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "REST corepressor" encoded by a nucleic acid that hybridizes to the "REST corepressor" nucleic acid or its complement under low stringency conditions, and/or

(xv) "S-100 alpha" (SEQ ID No:296) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions, and/or

(xvi) "S-100 beta" (SEQ ID No:304) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 beta" encoded by a nucleic acid that hybridizes to the "S-100 beta" nucleic acid or its complement under low stringency conditions, and/or

(xvii) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions, is present in the complex.

32. The method of any of No. 26 - 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 - 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

34. A method for the production of a pharmaceutical composition comprising carrying out the method of any of No. 1 - 8 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.

35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, activity of, or component composition of, or intracellular localization of the complex of any one of the No. 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in an analogous sample from a subject not having the disease or disorder or predisposition indicates the presence in the subject of the disease or disorder or predisposition in the subject.

36. The method of No. 35, wherein the amount of said complex is determined.

37. The method of No. 35, wherein the activity of said complex is determined.

38. The method of No. 37, wherein said determining step comprises isolating from the subject said complex to produce said isolated complex and contacting said isolated

complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.

39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.

40. The method of No. 39, wherein said determining step comprises determining whether (i) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions, and/or

(ii) "APP-C99" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP-C99" encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid or its complement under low stringency conditions, and/or

(iii) "CAMK2D" (SEQ ID No:297) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CAMK2D" encoded by a nucleic acid that hybridizes to the "CAMK2D" nucleic acid or its complement under low stringency conditions, and/or

(iv) "Delta-like homolog" (SEQ ID No:298) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-like homolog" encoded by a nucleic acid that hybridizes to the "Delta-like homolog" nucleic acid or its complement under low stringency conditions, and/or

(v) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions, and/or

(vi) "Fe65L1" (SEQ ID No:292) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions, and/or

- (vii) "Integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "Integral membrane transporter protein" nucleic acid or its complement under low stringency conditions, and/or
- (viii) "KIAA1102 (Fragment)" (SEQ ID No:285) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "KIAA1949" (SEQ ID No:299) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1949" encoded by a nucleic acid that hybridizes to the "KIAA1949" nucleic acid or its complement under low stringency conditions, and/or
- (x) "MGC4022" (SEQ ID No:300) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4022" encoded by a nucleic acid that hybridizes to the "MGC4022" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "MGC5442" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions, and/or
- (xii) "NAP-1 related protein" (SEQ ID No:301) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NAP-1 related protein" encoded by a nucleic acid that hybridizes to the "NAP-1 related protein" nucleic acid or its complement under low stringency conditions, and/or
- (xiii) "Neurocalcin delta" (SEQ ID No:302) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurocalcin delta" encoded by a nucleic acid that hybridizes to the "Neurocalcin delta" nucleic acid or its complement under low stringency conditions, and/or
- (xiv) "REST corepressor" (SEQ ID No:303) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "REST corepressor" encoded by a nucleic acid that hybridizes to the "REST corepressor" nucleic acid or its complement under low stringency conditions, and/or

(xv) "S-100 alpha" (SEQ ID No:296) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions, and/or

(xvi) "S-100 beta" (SEQ ID No:304) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 beta" encoded by a nucleic acid that hybridizes to the "S-100 beta" nucleic acid or its complement under low stringency conditions, and/or

(xvii) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions, is present in the complex.

41. The complex of any one of No. 1 - 8, or proteins of No. 13 or the antibody or fragment of No. 17, for use in a method of diagnosing a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity or component composition of or intracellular localization of, the complex of anyone of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting

proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), or protein components of, said complex.

43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.

44. The method according to No. 42, wherein said disease or disorder involves increased levels of the amount or activity of said complex.

45. Complex of any of No. 1 - 8 and/or protein selected from the following proteins

(i) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,

(ii) "APP-C99" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP-C99" encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid or its complement under low stringency conditions,

(iii) "CAMK2D" (SEQ ID No:297) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CAMK2D" encoded by a nucleic acid that hybridizes to the "CAMK2D" nucleic acid or its complement under low stringency conditions,

(iv) "Delta-like homolog" (SEQ ID No:298) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-like homolog" encoded by a nucleic acid that hybridizes to the "Delta-like homolog" nucleic acid or its complement under low stringency conditions,

(v) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,

(vi) "Fe65L1" (SEQ ID No:292) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions,

- (vii) "Integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "Integral membrane transporter protein" nucleic acid or its complement under low stringency conditions,
- (viii) "KIAA1102 (Fragment)" (SEQ ID No:285) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions,
- (ix) "KIAA1949" (SEQ ID No:299) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1949" encoded by a nucleic acid that hybridizes to the "KIAA1949" nucleic acid or its complement under low stringency conditions,
- (x) "MGC4022" (SEQ ID No:300) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4022" encoded by a nucleic acid that hybridizes to the "MGC4022" nucleic acid or its complement under low stringency conditions,
- (xi) "MGC5442" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions,
- (xii) "NAP-1 related protein" (SEQ ID No:301) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NAP-1 related protein" encoded by a nucleic acid that hybridizes to the "NAP-1 related protein" nucleic acid or its complement under low stringency conditions,
- (xiii) "Neurocalcin delta" (SEQ ID No:302) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurocalcin delta" encoded by a nucleic acid that hybridizes to the "Neurocalcin delta" nucleic acid or its complement under low stringency conditions,
- (xiv) "REST corepressor" (SEQ ID No:303) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "REST corepressor" encoded by a nucleic acid that hybridizes to the "REST corepressor" nucleic acid or its complement under low stringency conditions,

- (xv) "S-100 alpha" (SEQ ID No:296) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions,
- (xvi) "S-100 beta" (SEQ ID No:304) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 beta" encoded by a nucleic acid that hybridizes to the "S-100 beta" nucleic acid or its complement under low stringency conditions, and/or
- (xvii) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions, as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

The invention further relates to the following embodiments of the Tau-complex

1. A protein complex selected from complex (I) and comprising
  - (a) at least one first protein selected from the group consisting of:
    - (i) "14-3-3 protein zeta/delta" (SEQ ID No:6) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein zeta/delta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein zeta/delta" nucleic acid or its complement under low stringency conditions,
    - (ii) "Actin" (SEQ ID No:305) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Actin" encoded by a nucleic acid that hybridizes to the "Actin" nucleic acid or its complement under low stringency conditions,
    - (iii) "Alpha tubulin" (SEQ ID No:306) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Alpha tubulin" encoded by a nucleic acid that hybridizes to the "Alpha tubulin" nucleic acid or its complement under low stringency conditions,
    - (iv) "Beta tubulin" (SEQ ID No:307) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Beta tubulin"



encoded by a nucleic acid that hybridizes to the "Beta tubulin" nucleic acid or its complement under low stringency conditions,

(v) "PPP2CA (PP2A, catalytic subunit, alpha)" (SEQ ID No:312) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2CA (PP2A, catalytic subunit, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2CA (PP2A, catalytic subunit, alpha)" nucleic acid or its complement under low stringency conditions,

(vi) "PPP2CB (PP2A, catalytic subunit, beta)" (SEQ ID No:313) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2CB (PP2A, catalytic subunit, beta)" encoded by a nucleic acid that hybridizes to the "PPP2CB (PP2A, catalytic subunit, beta)" nucleic acid or its complement under low stringency conditions,

(vii) "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" (SEQ ID No:314) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" nucleic acid or its complement under low stringency conditions,

(viii) "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" nucleic acid or its complement under low stringency conditions, and

(ix) "Tau" (SEQ ID No:315) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Tau" encoded by a nucleic acid that hybridizes to the "Tau" nucleic acid or its complement under low stringency conditions, and

(b) at least one second protein, which second protein is selected from the group consisting of:

(i) "Deoxyhypusine synthase" (SEQ ID No:308) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Deoxyhypusine synthase" encoded by a nucleic acid that hybridizes to the "Deoxyhypusine synthase" nucleic acid or its complement under low stringency conditions,

- (ii) "Dynactin 2" (SEQ ID No:309) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynactin 2" encoded by a nucleic acid that hybridizes to the "Dynactin 2" nucleic acid or its complement under low stringency conditions,
- (iii) "MEP50" (SEQ ID No:310) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MEP50" encoded by a nucleic acid that hybridizes to the "MEP50" nucleic acid or its complement under low stringency conditions,
- (iv) "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" (SEQ ID No:311) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" encoded by a nucleic acid that hybridizes to the "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" nucleic acid or its complement under low stringency conditions, and
- (v) "S-100 beta" (SEQ ID No:304) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 beta" encoded by a nucleic acid that hybridizes to the "S-100 beta" nucleic acid or its complement under low stringency conditions, and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

2. The protein complex according to No. 1 wherein the first protein is the protein Tau (SEQ ID NO. 315), or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of 'Tau' encoded by a nucleic acid that hybridizes to the 'Tau' under low stringency conditions.

3. The protein complex according to No. 1 selected from complex (I) and comprising the following proteins:

- (i) "14-3-3 protein zeta/delta" (SEQ ID No:6) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein zeta/delta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein zeta/delta" nucleic acid or its complement under low stringency conditions,
- (ii) "Actin" (SEQ ID No:305) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Actin" encoded by a nucleic acid that hybridizes to the "Actin" nucleic acid or its complement under low stringency conditions,
- (iii) "Alpha tubulin" (SEQ ID No:306) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Alpha tubulin" encoded by a nucleic acid that hybridizes to the "Alpha tubulin" nucleic acid or its complement under low stringency conditions,
- (iv) "Beta tubulin" (SEQ ID No:307) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Beta tubulin" encoded by a nucleic acid that hybridizes to the "Beta tubulin" nucleic acid or its complement under low stringency conditions,
- (v) "Deoxyhypusine synthase" (SEQ ID No:308) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Deoxyhypusine synthase" encoded by a nucleic acid that hybridizes to the "Deoxyhypusine synthase" nucleic acid or its complement under low stringency conditions,
- (vi) "Dynactin 2" (SEQ ID No:309) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynactin 2" encoded by a nucleic acid that hybridizes to the "Dynactin 2" nucleic acid or its complement under low stringency conditions,
- (vii) "MEP50" (SEQ ID No:310) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MEP50" encoded by a nucleic acid that hybridizes to the "MEP50" nucleic acid or its complement under low stringency conditions,
- (viii) "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" (SEQ ID No:311) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" encoded by a nucleic acid that hybridizes to the "Nuclear receptor co-

repressor/HDAC3 complex subunit TBLR1" nucleic acid or its complement under low stringency conditions,

(ix) "PPP2CA (PP2A, catalytic subunit, alpha)" (SEQ ID No:312) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2CA (PP2A, catalytic subunit, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2CA (PP2A, catalytic subunit, alpha)" nucleic acid or its complement under low stringency conditions,

(x) "PPP2CB (PP2A, catalytic subunit, beta)" (SEQ ID No:313) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2CB (PP2A, catalytic subunit, beta)" encoded by a nucleic acid that hybridizes to the "PPP2CB (PP2A, catalytic subunit, beta)" nucleic acid or its complement under low stringency conditions,

(xi) "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" (SEQ ID No:314) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" nucleic acid or its complement under low stringency conditions,

(xii) "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" nucleic acid or its complement under low stringency conditions,

(xiii) "S-100 beta" (SEQ ID No:304) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 beta" encoded by a nucleic acid that hybridizes to the "S-100 beta" nucleic acid or its complement under low stringency conditions, and/or

(xiv) "Tau" (SEQ ID No:315) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Tau" encoded by a nucleic acid that hybridizes to the "Tau" nucleic acid or its complement under low stringency conditions.

4. The protein complex according to No. 1 comprising all but 1 - 4 of the following proteins:

- (i) "14-3-3 protein zeta/delta" (SEQ ID No:6) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein zeta/delta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein zeta/delta" nucleic acid or its complement under low stringency conditions,
- (ii) "Actin" (SEQ ID No:305) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Actin" encoded by a nucleic acid that hybridizes to the "Actin" nucleic acid or its complement under low stringency conditions,
- (iii) "Alpha tubulin" (SEQ ID No:306) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Alpha tubulin" encoded by a nucleic acid that hybridizes to the "Alpha tubulin" nucleic acid or its complement under low stringency conditions,
- (iv) "Beta tubulin" (SEQ ID No:307) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Beta tubulin" encoded by a nucleic acid that hybridizes to the "Beta tubulin" nucleic acid or its complement under low stringency conditions,
- (v) "Deoxyhypusine synthase" (SEQ ID No:308) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Deoxyhypusine synthase" encoded by a nucleic acid that hybridizes to the "Deoxyhypusine synthase" nucleic acid or its complement under low stringency conditions,
- (vi) "Dynactin 2" (SEQ ID No:309) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynactin 2" encoded by a nucleic acid that hybridizes to the "Dynactin 2" nucleic acid or its complement under low stringency conditions,
- (vii) "MEP50" (SEQ ID No:310) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MEP50" encoded by a nucleic acid that hybridizes to the "MEP50" nucleic acid or its complement under low stringency conditions,
- (viii) "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" (SEQ ID No:311) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" encoded by a nucleic acid that hybridizes to the "Nuclear receptor co-

repressor/HDAC3 complex subunit TBLR1" nucleic acid or its complement under low stringency conditions,

(ix) "PPP2CA (PP2A, catalytic subunit, alpha)" (SEQ ID No:312) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2CA (PP2A, catalytic subunit, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2CA (PP2A, catalytic subunit, alpha)" nucleic acid or its complement under low stringency conditions,

(x) "PPP2CB (PP2A, catalytic subunit, beta)" (SEQ ID No:313) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2CB (PP2A, catalytic subunit, beta)" encoded by a nucleic acid that hybridizes to the "PPP2CB (PP2A, catalytic subunit, beta)" nucleic acid or its complement under low stringency conditions,

(xi) "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" (SEQ ID No:314) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" nucleic acid or its complement under low stringency conditions,

(xii) "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" nucleic acid or its complement under low stringency conditions,

(xiii) "S-100 beta" (SEQ ID No:304) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 beta" encoded by a nucleic acid that hybridizes to the "S-100 beta" nucleic acid or its complement under low stringency conditions,

(xiv) "Tau" (SEQ ID No:315) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Tau" encoded by a nucleic acid that hybridizes to the "Tau" nucleic acid or its complement under low stringency conditions.

5. The complex of any of No. 1 - 4 comprising a functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein, respectively.
6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.
7. The complex of any of No. 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.
8. The complex of any of No. 1 - 7 that is involved in the the phosphorylation of tau proteins in vitro or in cells (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or the aggregation of tau proteins into filaments or tangles in vitro or in cells (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)).
9. A process for preparing a complex of any of No. 1 - 8 and optionally the components thereof comprising the following steps:expressing a protein (bait) of the complex, preferably a tagged protein, in a target cell, isolating the protein complex which is attached to the bait protein, and optionally dissociating the protein complex and isolating the individual complex members.
10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.
11. The process according to any of No. 9 - 10 wherein the two tags are separated by a cleavage site for a protease.

12. Component of the Tau complex obtainable by a process according to any of No. 9 - 11.

13. Protein of the Tau complex selected from

(i) "MEP50" (SEQ ID No:310) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MEP50" encoded by a nucleic acid that hybridizes to the "MEP50" nucleic acid or its complement under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

14. Nucleic acid encoding a protein according to No. 13.

15. Construct, preferably a vector construct, comprising (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or

(b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative of at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the second group of proteins according to No. 1 (b).

16. Host cell, containing a vector comprising at least one of the nucleic acid of No. 14 and/or a construct of No. 15 or containing several vectors each comprising at least the nucleic acid sequence encoding at least one of the proteins, or functionally active fragments or functionally active derivatives thereof selected from the first group of proteins according to No. 1 (a) and the proteins, or functionally active fragments or



functionally active derivatives thereof selected from the second group of proteins according to No. 1 (b).

17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody which binds to any of the proteins according to No. 13.

18. A kit comprising in one or more container the complex of any of No. 1 - 8 and/or the proteins of No. 13 optionally together with an antibody according to No. 17 and/or further components such as reagents and working instructions.

19. The kit according to No. 18 for processing a substrate of said complex.

20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

21. Array, in which at least a complex according to any of No. 1 - 8 and/or at least one protein according to No. 14 and/or at least one antibody according to No. 17 is attached to a solid carrier.

22. A process for processing a physiological substrate of the complex comprising the step of bringing into contact a complex to any of No. 1 - 8 with said substrate, such that said substrate is processed.

23. A pharmaceutical composition comprising the protein complex of any of No. 1 - 8 and/or any of the following the proteins:

(i) "MEP50" (SEQ ID No:310) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MEP50" encoded by a nucleic acid that hybridizes to the "MEP50" nucleic acid or its complement under low stringency conditions, and a pharmaceutical acceptable carrier.

24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

25. A method for screening for a molecule that binds to the complex of anyone of No. 1 - 8 and/or any of the following the proteins:

(i) "MEP50" (SEQ ID No:310) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MEP50" encoded by a nucleic acid that hybridizes to the "MEP50" nucleic acid or its complement under low stringency conditions, comprising the steps of

(a) exposing said complex, or a cell or organism containing same to one or more candidate molecules; and

(b) determining whether said candidate molecule is bound to the complex or protein.

26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 - 8 comprising the steps of (a) exposing said complex, or a cell or organism containing Tau complex to one or more candidate molecules; and

(b) determining the amount of activity of protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.

27. The method of No. 26, wherein the amount of said complex is determined.

28. The method of No. 26, wherein the activity of said complex is determined.

29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining the processing of said substrate is modified in the presence of said candidate molecule.

30. The method of No. 26, wherein the amount of the individual protein components of said complex are determined.

31. The method of No. 30, wherein said determining step comprises determining whether

- (i) "14-3-3 protein zeta/delta" (SEQ ID No:6) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein zeta/delta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein zeta/delta" nucleic acid or its complement under low stringency conditions, and/or
- (ii) "Actin" (SEQ ID No:305) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Actin" encoded by a nucleic acid that hybridizes to the "Actin" nucleic acid or its complement under low stringency conditions, and/or
- (iii) "Alpha tubulin" (SEQ ID No:306) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Alpha tubulin" encoded by a nucleic acid that hybridizes to the "Alpha tubulin" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "Beta tubulin" (SEQ ID No:307) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Beta tubulin" encoded by a nucleic acid that hybridizes to the "Beta tubulin" nucleic acid or its complement under low stringency conditions, and/or
- (v) "Deoxyhypusine synthase" (SEQ ID No:308) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Deoxyhypusine synthase" encoded by a nucleic acid that hybridizes to the "Deoxyhypusine synthase" nucleic acid or its complement under low stringency conditions, and/or

- (vi) "Dynactin 2" (SEQ ID No:309) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynactin 2" encoded by a nucleic acid that hybridizes to the "Dynactin 2" nucleic acid or its complement under low stringency conditions, and/or
- (vii) "MEP50" (SEQ ID No:310) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MEP50" encoded by a nucleic acid that hybridizes to the "MEP50" nucleic acid or its complement under low stringency conditions, and/or
- (viii) "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" (SEQ ID No:311) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" encoded by a nucleic acid that hybridizes to the "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "PPP2CA (PP2A, catalytic subunit, alpha)" (SEQ ID No:312) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2CA (PP2A, catalytic subunit, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2CA (PP2A, catalytic subunit, alpha)" nucleic acid or its complement under low stringency conditions, and/or
- (x) "PPP2CB (PP2A, catalytic subunit, beta)" (SEQ ID No:313) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2CB (PP2A, catalytic subunit, beta)" encoded by a nucleic acid that hybridizes to the "PPP2CB (PP2A, catalytic subunit, beta)" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" (SEQ ID No:314) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" nucleic acid or its complement under low stringency conditions, and/or
- (xii) "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2RBA, (PP2A, 55 KDA

regulatory subunit B, alpha)" nucleic acid or its complement under low stringency conditions, and/or

(xiii) "S-100 beta" (SEQ ID No:304) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 beta" encoded by a nucleic acid that hybridizes to the "S-100 beta" nucleic acid or its complement under low stringency conditions, and/or

(xiv) "Tau" (SEQ ID No:315) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Tau" encoded by a nucleic acid that hybridizes to the "Tau" nucleic acid or its complement under low stringency conditions, is present in the complex.

32. The method of any of No. 26 - 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 - 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

34. A method for the production of a pharmaceutical composition comprising carrying out the method of any of No. 1 - 8 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.

35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, activity of, or component composition of, or intracellular localization of the complex of any one of the No. 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity,

or protein components of, said complex in an analogous sample from a subject not having the disease or disorder or predisposition indicates the presence in the subject of the disease or disorder or predisposition in the subject.

36. The method of No. 35, wherein the amount of said complex is determined.

37. The method of No. 35, wherein the activity of said complex is determined.

38. The method of No. 37, wherein said determining step comprises isolating from the subject said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.

39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.

40. The method of No. 39, wherein said determining step comprises determining whether

- (i) "14-3-3 protein zeta/delta" (SEQ ID No:6) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein zeta/delta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein zeta/delta" nucleic acid or its complement under low stringency conditions, and/or
- (ii) "Actin" (SEQ ID No:305) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Actin" encoded by a nucleic acid that hybridizes to the "Actin" nucleic acid or its complement under low stringency conditions, and/or
- (iii) "Alpha tubulin" (SEQ ID No:306) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Alpha tubulin" encoded by a nucleic acid that hybridizes to the "Alpha tubulin" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "Beta tubulin" (SEQ ID No:307) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Beta tubulin"

encoded by a nucleic acid that hybridizes to the "Beta tubulin" nucleic acid or its complement under low stringency conditions, and/or

(v) "Deoxyhypusine synthase" (SEQ ID No:308) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Deoxyhypusine synthase" encoded by a nucleic acid that hybridizes to the "Deoxyhypusine synthase" nucleic acid or its complement under low stringency conditions, and/or

(vi) "Dynactin 2" (SEQ ID No:309) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynactin 2" encoded by a nucleic acid that hybridizes to the "Dynactin 2" nucleic acid or its complement under low stringency conditions, and/or

(vii) "MEP50" (SEQ ID No:310) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MEP50" encoded by a nucleic acid that hybridizes to the "MEP50" nucleic acid or its complement under low stringency conditions, and/or

(viii) "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" (SEQ ID No:311) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" encoded by a nucleic acid that hybridizes to the "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" nucleic acid or its complement under low stringency conditions, and/or

(ix) "PPP2CA (PP2A, catalytic subunit, alpha)" (SEQ ID No:312) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2CA (PP2A, catalytic subunit, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2CA (PP2A, catalytic subunit, alpha)" nucleic acid or its complement under low stringency conditions, and/or

(x) "PPP2CB (PP2A, catalytic subunit, beta)" (SEQ ID No:313) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2CB (PP2A, catalytic subunit, beta)" encoded by a nucleic acid that hybridizes to the "PPP2CB (PP2A, catalytic subunit, beta)" nucleic acid or its complement under low stringency conditions, and/or

(xi) "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" (SEQ ID No:314) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)"

encoded by a nucleic acid that hybridizes to the "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" nucleic acid or its complement under low stringency conditions, and/or (xii) "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" nucleic acid or its complement under low stringency conditions, and/or

(xiii) "S-100 beta" (SEQ ID No:304) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 beta" encoded by a nucleic acid that hybridizes to the "S-100 beta" nucleic acid or its complement under low stringency conditions, and/or

(xiv) "Tau" (SEQ ID No:315) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Tau" encoded by a nucleic acid that hybridizes to the "Tau" nucleic acid or its complement under low stringency conditions, is present in the complex.

41. The complex of any one of No. 1 - 8, or proteins of No. 13 or the antibody or fragment of No. 17, for use in a method of diagnosing a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity or component composition of or intracellular localization of, the complex of anyone of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, the phosphorylation of tau proteins in vitro or in cells (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or the aggregation of tau proteins into filaments or tangles in vitro or in cells (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), or protein components of, said complex.



43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.

44. The method according to No. 42, wherein said disease or disorder involves increased levels of the amount or activity of said complex.

45. Complex of any of No. 1 - 8 and/or protein selected from the following proteins

(i) "14-3-3 protein zeta/delta" (SEQ ID No:6) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein zeta/delta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein zeta/delta" nucleic acid or its complement under low stringency conditions,

(ii) "Actin" (SEQ ID No:305) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Actin" encoded by a nucleic acid that hybridizes to the "Actin" nucleic acid or its complement under low stringency conditions,

(iii) "Alpha tubulin" (SEQ ID No:306) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Alpha tubulin" encoded by a nucleic acid that hybridizes to the "Alpha tubulin" nucleic acid or its complement under low stringency conditions,

(iv) "Beta tubulin" (SEQ ID No:307) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Beta tubulin" encoded by a nucleic acid that hybridizes to the "Beta tubulin" nucleic acid or its complement under low stringency conditions,

(v) "Deoxyhypusine synthase" (SEQ ID No:308) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Deoxyhypusine synthase" encoded by a nucleic acid that hybridizes to the "Deoxyhypusine synthase" nucleic acid or its complement under low stringency conditions,

(vi) "Dynactin 2" (SEQ ID No:309) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynactin 2" encoded by a nucleic acid that hybridizes to the "Dynactin 2" nucleic acid or its complement under low stringency conditions,

(vii) "MEP50" (SEQ ID No:310) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MEP50" encoded by a

nucleic acid that hybridizes to the "MEP50" nucleic acid or its complement under low stringency conditions,

(viii) "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" (SEQ ID No:311) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" encoded by a nucleic acid that hybridizes to the "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" nucleic acid or its complement under low stringency conditions,

(ix) "PPP2CA (PP2A, catalytic subunit, alpha)" (SEQ ID No:312) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2CA (PP2A, catalytic subunit, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2CA (PP2A, catalytic subunit, alpha)" nucleic acid or its complement under low stringency conditions,

(x) "PPP2CB (PP2A, catalytic subunit, beta)" (SEQ ID No:313) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2CB (PP2A, catalytic subunit, beta)" encoded by a nucleic acid that hybridizes to the "PPP2CB (PP2A, catalytic subunit, beta)" nucleic acid or its complement under low stringency conditions,

(xi) "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" (SEQ ID No:314) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" nucleic acid or its complement under low stringency conditions,

(xii) "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" nucleic acid or its complement under low stringency conditions,

(xiii) "S-100 beta" (SEQ ID No:304) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 beta" encoded by a nucleic acid that hybridizes to the "S-100 beta" nucleic acid or its complement under low stringency conditions, and/or (xiv) "Tau" (SEQ ID No:315) or a functionally active derivative thereof, or a functionally active fragment thereof, or a

homolog thereof, or a variant of "Tau" encoded by a nucleic acid that hybridizes to the "Tau" nucleic acid or its complement under low stringency conditions, as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

## 5. PROTOCOLS:

The TAP-technology, which is more fully described in EP 1 105 508 B1 and in Rigaut, et al., 1999, Nature Biotechnol. 17:1030-1032 respectively was used and further adapted as described below for protein purification. Proteins were identified using mass spectrometry as described further below.

### 5.1 Construction of TAP-tagged bait

The cDNAs encoding the complete ORF were obtained by RT-PCR. Total RNA was prepared from appropriate cell lines using the RNeasy Mini Kit (Qiagen). Both cDNA synthesis and PCR were performed with the SUPERScript One-Step RT-PCR for Long templates Kit (Life Technologies) using gene-specific primers. After 35-40 cycles of amplification PCR-products with the expected size were gel-purified with the MinElute PCR Purification Kit (Qiagen) and, if necessary, used for further amplification. Low-abundant RNAs were amplified by nested PCR before gel-purification. Restriction sites for NotI were attached to PCR primers to allow subcloning of amplified cDNAs into the retroviral vectors pLE94-N/C-TAP thereby generating N- or C-terminal fusions with the TAP-tag (Rigaut et al., 1999, Nature Biotechnol. 17:1030-1032). N-terminal tagging was chosen for the following baits/entry points: Presenilin 2, Aph-1a, Pen-2, APP, Tau, Fe65. C-terminal tagging was chosen for the following baits/entry points: Nicastrin, Aph-1a, Aph-1b, APP695SW, APP-C99, Fe65, X11beta.

Clones were analyzed by restriction digest, DNA sequencing and by in vitro translation using the TNT T7 Quick Coupled Transcription/Translation System (Promega inc.). The presence of the proteins was proven by Western blotting using the protein A

part of the TAP-tag for detection. Briefly, separation of proteins by standard SDS-PAGE was followed by semi-dry transfer onto a nitrocellulose membrane (PROTRAN, Schleicher&Schuell) using the MultiphorII blotting apparatus from Pharmacia Biotech. The transfer buffer consisted of 48 mM Tris, 39 mM glycine, 10% methanol and 0,0375% sodium dodecylsulfate. After blocking in phosphate-buffered saline (PBS) supplemented with 10% dry milk powder and 0,1% Tween 20 transferred proteins were probed with the Peroxidase-Anti-Peroxidase Soluble Complex (Sigma) diluted in blocking solution. After intensive washing immunoreactive proteins were visualized by enhanced chemiluminescence (ECL; Amersham Pharmacia Biotech).

## **5.2 Preparation of Virus and infection**

As a vector, a MoMLV-based recombinant virus was used.

The preparation has been carried out as follows:

### **5.2.1 Preparation of Virus**

293 gp cells were grown to 100% confluency. They were split 1:5 on poly-L-Lysine plates (1:5 diluted poly-L-Lysine [0.01% stock solution, Sigma P-4832] in PBS, left on plates for at least 10 min.). On Day 2, 63 microgram of retroviral Vector DNA together with 13 microgram of DNA of plasmid encoding an appropriate envelope protein were transfected into 293 gp cells (Somia, et al., 1999, Proc. Natl. Acad. Sci. USA 96:12667-12672; Somia, et al. 2000, J. Virol. 74:4420-4424). On Day 3, the medium was replaced with 15 ml DMEM + 10% FBS per 15-cm dish. On Day 4, the medium containing viruses (supernatant) was harvested (at 24 h following medium change after transfection). When a second collection was planned, DMEM 10 % FBS was added to the plates and the plates were incubated for another 24 h. All collections were done as follows: The supernatant was filtered through 0.45 micrometer filter (Corning GmbH, cellulose acetate, 431155). The filter was placed into konical polyallomer centrifuge tubes (Beckman, 358126) that are placed in buckets of a SW 28 rotor (Beckman). The filtered supernatant was ultracentrifuged at 19400 rpm in the SW 28 rotor, for 2 hours at 21 degree Celsius. The supernatant was discarded. The pellet containing viruses was

resuspended in a small volume (for example 300 microliter) of Hank's Balanced Salt Solution [Gibco BRL, 14025-092], by pipetting up and down 100-times, using an aerosol-safe tip. The viruses were used for transfection as described below.

### 5.2.2 Infection

Cells that were infected were plated one day before into one well of a 6-well plate. 4 hours before infection, the old medium on the cells was replaced with fresh medium. Only a minimal volume was added, so that the cells are completely covered (e.g. 700 microliter). During infection, the cells were actively dividing.

A description of the cells and their growth conditions is given in 5.2.3

To the concentrated virus, polybrene (Hexadimethrine Bromide; Sigma, H 9268) was added to achieve a final concentration of 8 microgram/ml (this is equivalent to 2.4 microliter of the 1 milligram/ml polybrene stock per 300 microliter of concentrated retrovirus). The virus was incubated in polybrene at room temperature for 1 hour. For infection, the virus/polybrene mixture was added to the cells and incubated at 37 degree Celsius at the appropriate CO<sub>2</sub> concentration for several hours (e.g. over-day or over-night). Following infection, the medium on the infected cells was replaced with fresh medium. The cells were passaged as usual after they became confluent. The cells contain the retrovirus integrated into their chromosomes and stably express the gene of interest.

### 5.2.3 Cell lines

The following Cell-lines were used:

Fe65-complex: HEK-293-cells, SKN-BE2-cells, SH-SY5Y-cells; X11beta-complex: HEK-293-cells, SKN-BE2-cells, SH-SY5Y-cells; Psen-2-complex: SKN-BE2-cells, SH-SY5Y-cells, LAN-cells; Nicastrin-complex: HEK-293-cells, SKN-BE2-cells; Aph-1a-complex: HEK-293-cells, SKN-BE2-cells; Pen-2-complex: HEK-293-cells, SKN-BE2-cells;

APP695SW-complex: HEK-293-cells, SKN-BE2-cells; APP-C99-complex: SKN-BE2-cells; Tau-complex: SKN-BE2-cells, SH-SY5Y-cells

SKN-BE2 cells (American Type Culture Collection-No. CRL-2271) were grown in 95% OptiMEM + 5% iron-supplemented calf serum.

SH-SY5Y-cells were grown in 85% DMEM/F-12, 15% FBS, Non-essential AA

LAN-cells (human neuroblastoma cell line) were grown in 90% RPMI 1640 + 10% FBS

The expression pattern of the TAP-tagged proteins was checked by immunoblot-analysis as described in 5.3.3 and/or by immunofluorescence as described in 5.3.1 or 5.3.2.

### 5.3 Checking of expression pattern of TAP-tagged proteins

The expression pattern of the TAP-tagged protein was checked by immunoblot analysis and/or by immunofluorescence. Immunofluorescence analysis was either carried out according to section 5.3.1 or to section 5.3.2 depending on the type of the TAP-tagged protein. Immunoblot analysis was carried out according to section 5.3.3.

#### 5.3.1 Protocol for the indirect Immunofluorescence staining of fixed mammalian cells for plasma membrane and ER bound proteins

Cells were grown in FCS media on polylysine coated 8 well chamber slides to 50% confluency. Then fixation of the cells was performed in 4% ParaFormAldehyde diluted in Phosphate Buffer Saline (PBS) solution (0.14M Phosphate, 0.1M NaCl pH 7.4). The cells were incubated for 30 minutes at room temperature in 300 microliters per well. Quenching was performed in 0.1M Glycine in PBS for 2x 20 minutes at room temperature. Blocking was performed with 1% Bovine Serum Albumin (BSA) in 0.3% Saponin + PBS for at least 1 hour at room temperature. Incubation of the primary antibodies was performed in the blocking solution overnight at +4°C. The proper dilution of the antibodies was determined in a case to case basis. Cells were washed in PBS containing 0.3% Saponin for 2x 20 minutes at room temperature. Incubation of the

secondary antibodies is performed in the blocking solution. Alexa 594 coupled goat anti-rabbit is diluted 1:1000 (Molecular Probes). Alexa 488 coupled goat anti-mouse is diluted 1:1000 (Molecular Probes). DAPI was used to label DNA. If Phalloidin was used to label F-actin, the drug is diluted 1:500 and incubated with the secondary antibodies. Cells were then washed again 2x 20 minutes at room temperature in PBS. The excess of buffer was removed and cells were mounted in a media containing an anti-bleaching agent (Vectashield, Vector Laboratories).

### 5.3.2 Protocol for the indirect Immunofluorescence staining of fixed mammalian cells for non-plasma membrane bound proteins:

Cells were grown in FCS media on Polylysine coated 8 well chamber slides to 50% confluency. Fixation of the cells was performed in 4% ParaFormAldehyde diluted in Phosphate Buffer Saline (PBS) solution (0.14M Phosphate, 0.1M NaCl pH 7.4) for 30 minutes at Room Temperature (RT), 300 microliters per well. Quenching was performed in 0.1M Glycine in PBS for 2x 20 minutes at room temperature. Permeabilization of cells was done with 0.5% Triton X-100 in PBS for 10 minutes at room temperature. Blocking was then done in 1% Bovine Serum Albumin (BSA) in 0.3% Saponin + PBS for at least 1 hour at RT (Blocking solution). Incubation of the primary antibodies was performed in the blocking solution, overnight at +4°C. The proper dilution of the antibodies has to be determined in a case to case basis. Cells were washed in PBS containing 0.3% Saponin, for 2x 20 minutes at RT. Incubation of the secondary antibodies was performed in the blocking solution. Alexa 594 coupled goat anti-rabbit is diluted 1:1000 (Molecular Probes), Alexa 488 coupled goat anti-mouse is diluted 1:1000 (Molecular Probes). DAPI was used to label DNA. If Phalloidin is used to label F-actin, the drug is diluted 1:500 and incubated with the secondary antibodies. Cells were washed 2x 20 minutes at RT in PBS. The excess of buffer was removed and cells were mounted in a media containing an anti-bleaching agent (Vectashield, Vector Laboratories).

### 5.3.3 Immunoblot analysis

To analyze expression levels of TAP-tagged proteins, a cell pellet (from a 6-well dish) was lysed in 60  $\mu$ l DNase I buffer (5% Glycerol, 100 mM NaCl, 0.8 % NP-40 (IGEPAL), 5 mM magnesium sulfate, 100  $\mu$ g/ml DNase I (Roche Diagnostics), 50 mM Tris, pH 7.5, protease inhibitor cocktail) for 15 min on ice. Each sample was split into two aliquots. The first half was centrifuged at 13,000 rpm for 5 min. to yield the NP-40-extractable material in the supernatant; the second half (total material) was carefully triturated. 50  $\mu$ g each of the NP-40-extractable material and the total material are mixed with DTT-containing sample buffer for 30 min at 50°C on a shaker and separated by SDS polyacrylamide gel electrophoresis on a precast 4-12% Bis-Tris gel (Invitrogen). Proteins were then transferred to nitrocellulose using a semi-dry procedure with a discontinuous buffer system. Briefly, gel and nitrocellulose membrane were stacked between filter papers soaked in either anode buffer (three layers buffer A1 (0.3 M Tris-HCl) and three layers buffer A2 (0.03 M Tris-HCl)) or cathode buffer (three layers of 0.03 M Tris-HCl, pH 9.4, 0.1 % SDS, 40 mM  $\epsilon$ -aminocaproic acid). Electrotransfer of two gels at once was performed at 600 mA for 25 min. Transferred proteins were visualized with Ponceau S solution for one min to control transfer efficiency and then destained in water. The membrane was blocked in 5% non-fat milk powder in TBST (TBS containing 0.05% Tween-20) for 30 min at room temperature. It was subsequently incubated with HRP-coupled PAP antibody (1:5000 diluted in 5% milk/TBST) for 1 h at room temperature, washed three times for 10 min in TBST. The blot membrane was finally soaked in chemiluminescent substrate (ECL, Roche Diagnostics) for 2 min. and either exposed to X-ray film or analyzed on an imaging station.

#### 5.4 Purification of protein complexes

Protein complex purification was adapted to the sub-cellular localization of the TAP-tagged protein and was performed as described below.

##### 5.4.1 Lysate preparation for cytoplasmic proteins

About  $1 \times 10^9$  adherent cells (average) were harvested with a cell scraper and washed 3 times in ice-cold PBS (3 min, 550g). Collected cells were frozen in liquid



nitrogen or immediately processed further. For cell lysis, the cell pellet was resuspended in 10 ml of CZ lysis buffer (50 mM Tris-Cl, pH 7.4; 5 % Glycerol; 0,2 % IGEPAL; 1.5 mM  $MgCl_2$ ; 100 mM NaCl; 25 mM NaF; 1 mM  $Na_3VO_4$ ; 1 mM DTT; containing 1 tablet of EDTA-free Protease inhibitor cocktail (Complete™, Roche) per 25 ml of buffer) and homogenized by 10 strokes of a tight-fitted pestle in a dounce homogenizer. The lysate was incubated for 30 min on ice and spun for 10 min at 20,000g. The supernatant was subjected to an additional ultracentrifugation step for 1 h at 100,000g. The supernatant was recovered and rapidly frozen in liquid nitrogen or immediately processed further.

#### 5.4.2 Lysate preparation for membrane proteins

About  $1 \times 10^9$  adherent cells (average) were harvested with a cell scraper and washed 3 times in ice-cold PBS (3 min, 550g). Collected cells were frozen in liquid nitrogen or immediately processed further. For cell lysis, the cell pellet was resuspended in 10 ml of Membrane-Lysis buffer (50 mM Tris, pH 7.4; 7.5 % Glycerol; 1 mM EDTA; 150 mM NaCl; 25 mM NaF; 1 mM  $Na_3VO_4$ ; 1 mM DTT; containing 1 tablet of EDTA-free Protease inhibitor cocktail (Complete™, Roche) per 25 ml of buffer) and homogenized by 10 strokes of a tight-fitted pestle in a dounce homogenizer. The lysate was spun for 10 min at 750g, the supernatant was recovered and subjected to an ultracentrifugation step for 1 h at 100,000g. The membrane pellet was resuspended in 7,5 ml of Membrane-Lysis buffer containing 0.8% n-Dodecyl- $\beta$ -D-maltoside and incubated for 1 h at 4°C with constant agitation. The sample was subjected to another ultracentrifugation step for 1h at 100,000g and the solubilized material was quickly frozen in liquid nitrogen or immediately processed further.

#### 5.4.3 Lysate preparation for nuclear proteins

About  $1 \times 10^9$  adherent cells (average) were harvested with a cell scraper and washed 3 times in ice-cold PBS (3 min, 550g). Collected cells were frozen in liquid nitrogen or immediately processed further. For cell lysis, the cell pellet was resuspended in 10 ml of Hypotonic-Lysis buffer (10 mM Tris, pH 7.4; 1.5 mM  $MgCl_2$ ; 10 mM KCl; 25 mM NaF; 1 mM  $Na_3VO_4$ ; 1 mM DTT; containing 1 tablet of EDTA-free Protease inhibitor

cocktail (Complete™, Roche) per 25 ml of buffer) and homogenized by 10 strokes of a tight-fitted pestle in a dounce homogenizer. The lysate was spun for 10 min at 2,000g and the resulting supernatant (S1) saved on ice. The nuclear pellet (P1) was resuspended in 5 ml Nuclear-Lysis buffer (50 mM Tris, pH 7.4; 1.5 mM MgCl<sub>2</sub>; 20 % Glycerol; 420 mM NaCl; 25 mM NaF; 1 mM Na<sub>3</sub>VO<sub>4</sub>; 1 mM DTT; containing 1 tablet of EDTA-free Protease inhibitor cocktail (Complete™, Roche) per 25 ml of buffer) and incubated for 30 min on ice. The sample was combined with S1, further diluted with 7 ml of Dilution buffer (110 mM Tris, pH 7.4; 0.7 % NP40; 1.5 mM MgCl<sub>2</sub>; 25 mM NaF; 1 mM Na<sub>3</sub>VO<sub>4</sub>; 1 mM DTT), incubated on ice for 10 min and centrifuged at 100,000g for 1h. The final supernatant (S2) was frozen quickly in liquid nitrogen.

#### 5.4.4 Tandem Affinity Purification

The frozen lysate was quickly thawed in a 37°C water bath, and spun for 20 min at 100,000g. The supernatant was recovered and incubated with 0.2 ml of settled rabbit IgG-Agarose beads (Sigma) for 2 h with constant agitation at 4°C. Immobilized protein complexes were washed with 10 ml of CZ lysis buffer (containing 1 Complete™ tablet (Roche) per 50 ml of buffer) and further washed with 5 ml of TEV cleavage buffer (10 mM Tris, pH 7.4; 100 mM NaCl; 0.1 % IGEPAL; 0.5 mM EDTA; 1 mM DTT). Protein-complexes were eluted by incubation with 5 µl of TEV protease (GibcoBRL, Cat.No. 10127-017) for 1 h at 16°C in 150 µl TEV cleavage buffer. The eluate was recovered and combined with 0.2 ml settled Calmodulin affinity beads (Stratagene) in 0.2 ml CBP binding buffer (10 mM Tris, pH 7.4; 100 mM NaCl; 0.1 % IGEPAL; 2mM MgAc; 2mM Imidazole; 1mM DTT; 4 mM CaCl<sub>2</sub>) followed by 1 h incubation at 4°C with constant agitation. Immobilized protein complexes were washed with 10 ml of CBP wash buffer (10 mM Tris, pH 7.4; 100 mM NaCl; 0.1 % IGEPAL; 1mM MgAc; 1mM Imidazole; 1mM DTT; 2 mM CaCl<sub>2</sub>) and eluted by addition of 600 µl CBP elution buffer (10 mM Tris, pH 8.0; 5 mM EGTA) for 5 min at 37°C. The eluate was recovered in a siliconized tube and lyophilized. The remaining Calmodulin resin was boiled for 5 min in 50 µl 4x Laemmli sample buffer. The sample buffer was isolated, combined with the lyophilised fraction and loaded on a NuPAGE gradient gel (Invitrogen, 4-12%, 1.5 mm, 10 well).

#### 5.4.5 Isolation of the Sambiasin complex of the invention from mouse tissue

Two mouse forebrains (0.6314 g total wet weight) were lysed in 14 mls of 50 mM HEPES pH 7.4; 150 mM NaCl; 1 mM EDTA; 0.5 mM Sodium Vanadate; 10% Glycerol; 1% n-Dodecyl- $\beta$ -D-maltoside containing standard proteinase inhibitors. The tissue was homogenised in a Warring blender for 30 seconds on ice. Homogenates were incubated on ice for 1 hour and then centrifuged at 13,000 g for 30 min at 4°C. The resulting pellet was stored at -80°C while the supernatant was centrifuged at 50,000 g for 30 min at 4°C and the resulting pellet was also stored at -80°C. 6.5 ml of the supernatant from this second centrifugation step was taken and combined with 25  $\mu$ l of anti presenilin-1 antisera (MAB5232, Chemicon). The antibody/lysate mixture was incubated for 1 hour at 4°C with end-over end mixing. Pre-washed protein G sepharose was added and the mixture was incubated overnight at 4°C with end-over mixing. The protein G was recovered by centrifugation at 200 g for 5 min at 4°C. The protein G beads were then washed 5 times in 1ml lysis buffer (containing 0.1% n-Dodecyl- $\beta$ -D-maltoside rather than 1%). 100  $\mu$ l of NuPAGE sample buffer (Invitrogen) was added and the sample incubated at 37°C for 10 min. Samples were separated on 4-12 % NuPAGE bis/tris gels (Invitrogen, 1.5 mm, 10 well). Proteins were visualized by staining with colloidal coomassie (Sigma) and then analysed by LC/MSMS.

#### 5.5 Protein identification by mass spectrometry

##### 5.5.1 Protein digestion prior to mass spectrometric analysis

Gel-separated proteins were reduced, alkylated and digested in gel essentially following the procedure described by Shevchenko et al., 1996, Anal. Chem. 68:850-858. Briefly, gel-separated proteins were excised from the gel using a clean scalpel, reduced using 10 mM DTT (in 5mM ammonium bicarbonate, 54°C, 45 min) and subsequently alkylated with 55 mM iodoacetamid (in 5 mM ammonium bicarbonate) at room temperature in the dark (30 min). Reduced and alkylated proteins were digested in gel with porcine trypsin (Promega) at a protease concentration of 12.5 ng/ $\mu$ l in 5mM ammonium bicarbonate. Digestion was allowed to proceed for 4 hours at 37°C and the reaction was subsequently stopped using 5  $\mu$ l 5% formic acid.

### 5.5.2 Sample preparation prior to analysis by mass spectrometry

Gel plugs were extracted twice with 20  $\mu$ l 1% TFA and pooled with acidified digest supernatants. Samples were dried in a vacuum centrifuge and resuspended in 13  $\mu$ l 1% TFA.

### 5.5.3 Mass spectrometric data acquisition

Peptide samples were injected into a nano LC system (CapLC, Waters or Ultimate, Dionex) which was directly coupled either to a quadrupole TOF (QTOF2, QTOF Ultima, QTOF Micro, Micromass or QSTAR Pulsar, Sciex) or ion trap (LCQ Deca XP) mass spectrometer. Peptides were separated on the LC system using a gradient of aqueous and organic solvents (see below). Solvent A was 5% acetonitrile in 0.5% formic acid and solvent B was 70% acetonitrile in 0.5% formic acid.

Time (min)	% solvent A	% solvent B
0	95	5
5.33	92	8
35	50	50
36	20	80
40	20	80
41	95	5
50	95	5

Peptides eluting off the LC system were partially sequenced within the mass spectrometer.

### 5.5.4 Protein identification

The peptide mass and fragmentation data generated in the LC-MS/MS experiments were used to query fasta formatted protein and nucleotide sequence databases maintained and updated regularly at the NCBI (for the NCBI nr, dbEST and the

human and mouse genomes) and European Bioinformatics Institute (EBI, for the human, mouse, *D. melanogaster* and *C. elegans* proteome databases). Proteins were identified by correlating the measured peptide mass and fragmentation data with the same data computed from the entries in the database using the software tool Mascot (Matrix Science; Perkins et al., 1999, *Electrophoresis* 20:3551-3567). Search criteria varied depending on which mass spectrometer was used for the analysis.

TABLE 1

## COMPONENTS OF COMPLEXES

Name of complex	Entry Point	All interactors of the complex	Known interactors of the complex	Novel interactors of the complex	Proteins of unknown function
Fe65-complex	Fe65	APP	APP		
		14-3-3 protein epsilon		14-3-3 protein epsilon	
		14-3-3 protein beta/alpha		14-3-3 protein beta/alpha	
		14-3-3 protein eta		14-3-3 protein eta	
		14-3-3 protein gamma		14-3-3 protein gamma	
		14-3-3 protein tau		14-3-3 protein tau	
		14-3-3 protein zeta/delta		14-3-3 protein zeta/delta	
		APLP1	APLP1		
		APLP2	APLP2		
		APP-C99	APP-C99	APP-C99	APP-C99
		ATP-binding cassette, sub-family B, member 7		ATP-binding cassette, sub-family B, member 7	

	ECP-51		ECP-51	
	Fe65	Fe65		
	GAP-associated tyrosine phosphoprotein p62		GAP-associated tyrosine phosphoprotein p62	
	Integral membrane protein 2B (ITM2B)		Integral membrane protein 2B (ITM2B)	
	IPI00104084.1		IPI00104084.1	IPI00104084.1
	Krab box protein ensp00000302970		Krab box protein ensp00000302970	Krab box protein ensp00000302970
	PDZ domain protein MAGI-3		PDZ domain protein MAGI-3	
	PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)		PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)	
	Protein similar to probable mitotic centromere associated kinesin		Protein similar to probable mitotic centromere associated kinesin	Protein similar to probable mitotic centromere associated kinesin
	RNB6	RNB6		
	SAP-62		SAP-62	
	Transcription factor CP2	Transcription factor CP2		

		Zinc finger protein 277		Zinc finger protein 277	Zinc finger protein 277
X11b-complex	X11b	ADAMTS-19		ADAMTS-19	ADAMTS-19
		APLP1		APLP1	
		APP	APP		
		Axonemal dynein heavy chain 8		Axonemal dynein heavy chain 8	
		BAT1		BAT1	BAT1
		C20orf11 (sim to a region of RANBPM)		C20orf11 (sim to a region of RANBPM)	C20orf11 (sim to a region of RANBPM)
		Cadherin EGF LAG seven-pass G-type receptor 2		Cadherin EGF LAG seven-pass G-type receptor 2	Cadherin EGF LAG seven-pass G-type receptor 2
		Calsyntenin-1		Calsyntenin-1	
		Calsyntenin-2		Calsyntenin-2	Calsyntenin-2
		Calsyntenin-3		Calsyntenin-3	Calsyntenin-3
		CGB0_HUMAN		CGB0_HUMAN	CGB0_HUMAN
		Chondroitin sulfate proteoglycan 6		Chondroitin sulfate proteoglycan 6	
		Chromatin-specific transcription elongation		Chromatin-specific transcription elongation	



	factor FACT 140 kDa subunit		factor FACT 140 kDa subunit	
	DC6 protein		DC6 protein	
	Dkfp586c1924		Dkfp586c1924	Dkfp586c1924
	Dynein light chain 2A		Dynein light chain 2A	
	Dynein light chain-A		Dynein light chain-A	
	ELAVL3		ELAVL3	
	ENG00000168820 (hypothetical protein with p-loop)		ENG00000168820 (hypothetical protein with p-loop)	ENG00000168820 (hypothetical protein with p-loop)
	Eukaryotic translation initiation factor 4A, isoform		Eukaryotic translation initiation factor 4A, isoform	
	Filamin, gamma		Filamin, gamma	
	FLJ13910		FLJ13910	FLJ13910
	FRAP1		FRAP1	
	GTP-binding protein ERA		GTP-binding protein ERA	
	HADH2/ERAB (mitochondrial enzyme)		HADH2/ERAB (mitochondrial enzyme)	
	HDAC2		HDAC2	
	HERC2 protein		HERC2 protein	HERC2 protein

	HSPC154		HSPC154	HSPC154
	HSPC245		HSPC245	HSPC245
	Hunc18a	Hunc18a		
	HYPOTHETICAL PROTEIN FLJ10618		HYPOTHETICAL PROTEIN FLJ10618	HYPOTHETICAL PROTEIN FLJ10618
	Hypothetical protein FLJ10795		Hypothetical protein FLJ10795	
	HYPOTHETICAL PROTEIN FLJ12599.		HYPOTHETICAL PROTEIN FLJ12599.	HYPOTHETICAL PROTEIN FLJ12599.
	Hypothetical protein FLJ20397		Hypothetical protein FLJ20397	Hypothetical protein FLJ20397
	hypothetical protein MGC13186		hypothetical protein MGC13186	hypothetical protein MGC13186
	IKAP		IKAP	
	Insulinoma-glucagonoma protein 20		Insulinoma- glucagonoma protein 20	
	KIAA0056		KIAA0056	KIAA0056
	KIAA0166		KIAA0166	KIAA0166
	KIAA0325 (FRAGMENT)		KIAA0325 (FRAGMENT)	
	KIAA0564		KIAA0564	KIAA0564

	KIAA0763		KIAA0763	KIAA0763
	Laminin, gamma 1		Laminin, gamma 1	
	LIB ( leucine-rich repeat protein)		LIB ( leucine-rich repeat protein)	
	MBIP		MBIP	
	MEGF7 (FRAGMENT)		MEGF7 (FRAGMENT)	MEGF7 (FRAGMENT)
	MT-ACT48		MT-ACT48	MT-ACT48
	Myosin IXB		Myosin IXB	
	NEU1		NEU1	
	Neurexin-1	Neurexin-1		
	NIPSNAP1		NIPSNAP1	NIPSNAP1
	NIPSNAP2		NIPSNAP2	
	Paladin		Paladin	Paladin
	PDZ and LIM domain protein 1		PDZ and LIM domain protein 1	PDZ and LIM domain protein 1
	Phosphoenolpyruvate carboxykinase 2 (mitochondrial)		Phosphoenolpyruvate carboxykinase 2 (mitochondrial)	
	PILB		PILB	PILB
	PILT		PILT	PILT
	Procollagen C-		Procollagen C-	

	endopeptidase enhancer		endopeptidase enhancer	
	Programmed cell death 10		Programmed cell death 10	Programmed cell death 10
	Protein similar to AGCP6688		Protein similar to AGCP6688	Protein similar to AGCP6688
	RAB7L1		RAB7L1	RAB7L1
	RANBP1		RANBP1	
	Reelin		Reelin	
	RPGR-interacting protein 1		RPGR-interacting protein 1	
	Serine/threonine phosphatase 6		Serine/threonine phosphatase 6	
	similar to SD27354p [Drosophila melanogaster]		similar to SD27354p [Drosophila melanogaster]	similar to SD27354p [Drosophila melanogaster]
	SNAP-25	SNAP-25		
	Sortilin-related receptor		Sortilin-related receptor	
	STMN3		STMN3	
	STX1A	STX1A		
	SUCLA2		SUCLA2	
	Synaptogyrin 3		Synaptogyrin 3	

		TYK2		TYK2	
		Ubiquitin-protein ligase E3-alpha		Ubiquitin-protein ligase E3-alpha	Ubiquitin-protein ligase E3-alpha
		VGF nerve growth factor inducible protein		VGF nerve growth factor inducible protein	
		X11beta	X11beta		
		Zinc finger protein 198		Zinc finger protein 198	
PSEN2-complex	PSEN2	18 kDa microsomal signal peptidase subunit		18 kDa microsomal signal peptidase subunit	
		200 kDa proteasome activator		200 kDa proteasome activator	
		ABCB11		ABCB11	
		Acetolactate synthase homolog		Acetolactate synthase homolog	
		Adrenoleukodystrophy protein		Adrenoleukodystrophy protein	
		Aph-1a	Aph-1a		
		ATM		ATM	
		ATP7A		ATP7A	
		ATP-binding cassette protein, sub-family B,		ATP-binding cassette protein, sub-family B,	

	member 1		member 1	
	ATP-dependent metalloprotease FtsH1 homolog		ATP-dependent metalloprotease FtsH1 homolog	
	BIG1		BIG1	
	BTAF1		BTAF1	
	Calcium-binding protein P22		Calcium-binding protein P22	
	Cation-chloride cotransporter-interacting protein		Cation-chloride cotransporter-interacting protein	
	CD97		CD97	
	CDM_HUMAN		CDM_HUMAN	CDM_HUMAN
	Centromere/kinetochore protein ZW10 homolog		Centromere/kinetochore protein ZW10 homolog	
	Cerebral protein 10		Cerebral protein 10	Cerebral protein 10
	CGI-13		CGI-13	CGI-13
	CGI-51		CGI-51	CGI-51
	cholinergic receptor, nicotinic, alpha polypeptide 3		cholinergic receptor, nicotinic, alpha polypeptide 3	

	CHRNA3		CHRNA3	
	DAAM1		DAAM1	
	DAPK1		DAPK1	
	DKFZp586c1924		DKFZp586c1924	DKFZp586c1924
	DOCK3		DOCK3	
	Down syndrome critical region protein 2		Down syndrome critical region protein 2	
	ECSIT		ECSIT	
	ensp00000297280 (hypothetical protein with p-loop)		ensp00000297280 (hypothetical protein with p-loop)	ensp00000297280 (hypothetical protein with p-loop)
	FACL1		FACL1	
	FLJ20342		FLJ20342	FLJ20342
	FLJ20420		FLJ20420	FLJ20420
	FLJ22555		FLJ22555	FLJ22555
	FLJ22678		FLJ22678	FLJ22678
	Galactosylgalactosyl- osylprotein 3-beta- glucuronosyltransferase 3		Galactosylgalactosyl- osylprotein 3-beta- glucuronosyltransferase e 3	
	HTRA2		HTRA2	
	HU-K4		HU-K4	

		Hypothetical protein FLJ23356		Hypothetical protein FLJ23356	Hypothetical protein FLJ23356
		Hypothetical protein KIAA0455		Hypothetical protein KIAA0455	Hypothetical protein KIAA0455
		Hypothetical protein KIAA0971-l		Hypothetical protein KIAA0971-l	Hypothetical protein KIAA0971-l
		HYPOTHETICAL PROTEIN XP_174405.		HYPOTHETICAL PROTEIN XP_174405.	HYPOTHETICAL PROTEIN XP_174405.
		KIAA0062 (FRAGMENT)		KIAA0062 (FRAGMENT)	KIAA0062 (FRAGMENT)
		KIAA0090		KIAA0090	KIAA0090
		KIAA0103		KIAA0103	KIAA0103
		MGC4248		MGC4248	MGC4248
		MGC5442		MGC5442	MGC5442
		Nicastrin	Nicastrin		
		NICE-3		NICE-3	NICE-3
		NPC1		NPC1	
		NPD002		NPD002	
		NPL4, a component of the nuclear pore complex		NPL4, a component of the nuclear pore complex	NPL4, a component of the nuclear pore complex



	P63 protein		P63 protein	
	Presenilin 2		Presenilin 2	
	Prohibitin		Prohibitin	
	PSMA1		PSMA1	
	PSMA3		PSMA3	
	PSMA4		PSMA4	
	PSMA6		PSMA6	
	PSMB1		PSMB1	
	PSMB2		PSMB2	
	PSMB3		PSMB3	
	PSMB4		PSMB4	
	PSMB5		PSMB5	
	PSMB6		PSMB6	
	PSMC1		PSMC1	
	PSMC2		PSMC2	
	PSMC3		PSMC3	
	PSMC4		PSMC4	
	PSMC5		PSMC5	
	PSMC6		PSMC6	
	PSMD1		PSMD1	
	PSMD11		PSMD11	
	PSMD12		PSMD12	

		PSMD13		PSMD13	
		PSMD2		PSMD2	
		PSMD3		PSMD3	
		PSMD4		PSMD4	
		RPS6KA3		RPS6KA3	
		Serine/threonine phosphatase 6		Serine/threonine protein phosphatase 6	
		SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10.		SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10.	SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10.
		Sortilin 1		Sortilin 1	
		Stearoyl-CoA desaturase		Stearoyl-CoA desaturase	
		STRA6 isoform 1		STRA6 isoform 1	STRA6 isoform 1
		Tparl		Tparl	Tparl
		Ubiquitin-protein ligase EDD		Ubiquitin-protein ligase EDD	
		Voltage-dependent anion channel 2		Voltage-dependent anion channel 2	
		Wolframin		Wolframin	
Nicastrin-	Nicastrin	18 kDa microsomal		18 kDa microsomal	

complex	signal peptidase subunit	signal peptidase subunit	signal peptidase subunit	
	25 kDa microsomal signal peptidase subunit		25 kDa microsomal signal peptidase subunit	
	Aph-1a	Aph-1a		
	ATP-binding cassette, sub-family A, member 3		ATP-binding cassette, sub-family A, member 3	ATP-binding cassette, sub-family A, member 3
	BACE1	BACE1		
	BSCv protein (FRAGMENT)		BSCv protein (FRAGMENT)	
	CAMK4		CAMK4	
	Casein kinase II beta chain		Casein kinase II beta chain	
	Cathepsin B		Cathepsin B	
	CGI-13		CGI-13	CGI-13
	DCTN1		DCTN1	
	Delta-6 fatty acid desaturase		Delta-6 fatty acid desaturase	
	ENSG00000144840		ENSG00000144840	ENSG00000144840
	FACL3		FACL3	

	FACL4		FACL4	
	FLJ13977		FLJ13977	
	FLJ20342		FLJ20342	FLJ20342
	FLJ20481		FLJ20481	FLJ20481
	FLJ22390		FLJ22390	FLJ22390
	homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)		homolog of yeast golgi membrane protein yip1p (yip1p-interacting factor)	
	ICAM-2		ICAM-2	
	KIAA0095		KIAA0095	KIAA0095
	KIAA0922		KIAA0922	KIAA0922
	KIAA1181 (FRAGMENT)		KIAA1181 (FRAGMENT)	KIAA1181 (FRAGMENT)
	KIAA1533 (FRAGMENT)		KIAA1533 (FRAGMENT)	KIAA1533 (FRAGMENT)
	Mesenchymal stem cell protein DSCD75		Mesenchymal stem cell protein DSCD75	
	Neurotrypsin		Neurotrypsin	
	Nicastrin	Nicastrin		
	NICE-3		NICE-3	
	PAS domain containing		PAS domain containing	

		serine/threonine kinase		serine/threonine kinase	
		Pen-2	Pen-2		
		PP1, regulatory subunit 15B		PP1, regulatory subunit 15B	PP1, regulatory subunit 15B
		Presenilin-1	Presenilin-1		
		Presenilin-2	Presenilin-2		
		Protein amplified in osteosarcoma (OS-9)		Protein amplified in osteosarcoma (OS-9)	
		Protein similar to stromal cell-derived factor 2		Protein similar to stromal cell-derived factor 2	
		Protocadherin beta 8		Protocadherin beta 8	
		REP8 protein		REP8 protein	
		Retinal short-chain dehydrogenase/reductase retSDR2		Retinal short-chain dehydrogenase/reductase retSDR2	
		RING finger protein 5		RING finger protein 5	RING finger protein 5
		Stromal cell-derived factor 2-like 1		Stromal cell-derived factor 2-like 1	
		Thioredoxin domain-containing protein		Thioredoxin domain-containing protein	Thioredoxin domain-containing protein
		tyrosine phosphatase		tyrosine phosphatase	tyrosine phosphatase

		ensg00000149185		ensg00000149185	ensg00000149185
Aph-1a-complex	Aph-1a	18 kDa microsomal signal peptidase subunit		18 kDa microsomal signal peptidase subunit	
		23 kDa microsomal signal peptidase		23 kDa microsomal signal peptidase	
		25 kDa microsomal signal peptidase subunit		25 kDa microsomal signal peptidase subunit	
		ABCC1		ABCC1	ABCC1
		Acetolactate synthase homolog		Acetolactate synthase homolog	Acetolactate synthase homolog
		APLP2		APLP2	
		Aph-1a	Aph-1a		
		APP		APP	
		ATM		ATM	
		ATP1B1		ATP1B1	
		ATP2C1		ATP2C1	
		ATP-binding cassette, sub-family A member 3		ATP-binding cassette, sub-family A member 3	ATP-binding cassette, sub-family A member 3
		Brain-specific GTP-		Brain-specific GTP-	

	binding protein		binding protein	
	CDW92		CDW92	CDW92
	Cerebral protein-10		Cerebral protein-10	Cerebral protein-10
	CGI-13		CGI-13	CGI-13
	CNTNAP1		CNTNAP1	
	Dihydrofolate reductase		Dihydrofolate reductase	
	DNM1		DNM1	
	Endocytic receptor Endo180		Endocytic receptor Endo180	
	ENG		ENG	
	EXT2		EXT2	
	EXTL3		EXTL3	
	FLJ13660		FLJ13660	
	GPR49		GPR49	GPR49
	HK2		HK2	
	HU-K4		HU-K4	
	HUNC18a		HUNC18a	
	HYPOTHETICAL PROTEIN		HYPOTHETICAL PROTEIN	HYPOTHETICAL PROTEIN
	Hypothetical protein (Fragment)		Hypothetical protein (Fragment)	Hypothetical protein (Fragment)

	Hypothetical protein FLJ14562		Hypothetical protein FLJ14562	Hypothetical protein FLJ14562
	Hypothetical protein FLJ23630		Hypothetical protein FLJ23630	Hypothetical protein FLJ23630
	Hypothetical protein KIAA0372		Hypothetical protein KIAA0372	Hypothetical protein KIAA0372
	hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5		hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5	hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5
	hypothetical protein MGC22916		hypothetical protein MGC22916	hypothetical protein MGC22916
	ICAM2		ICAM2	
	IGF2R		IGF2R	
	Insulinoma-glucagonoma protein 20		Insulinoma- glucagonoma protein 20	
	Integral membrane protein 2B (ITM2B)		Integral membrane protein 2B (ITM2B)	
	integral membrane transporter protein		integral membrane transporter protein	integral membrane transporter protein
	ITPR1		ITPR1	



	KIAA0062 (FRAGMENT)		KIAA0062 (FRAGMENT)	KIAA0062 (FRAGMENT)
	KIAA0251 (FRAGMENT)		KIAA0251 (FRAGMENT)	KIAA0251 (FRAGMENT)
	KIAA0363 (FRAGMENT)		KIAA0363 (FRAGMENT)	KIAA0363 (FRAGMENT)
	KIAA0763		KIAA0763	KIAA0763
	KIAA0971		KIAA0971	KIAA0971
	KIAA1250		KIAA1250	KIAA1250
	LRP5		LRP5	
	Mesenchymal stem cell protein DSCD75		Mesenchymal stem cell protein DSCD75	Mesenchymal stem cell protein DSCD75
	MGC4248		MGC4248	MGC4248
	Neurotrypsin		Neurotrypsin	
	Nicastrin	Nicastrin		
	NRP2		NRP2	
	PCDHA10		PCDHA10	PCDHA10
	PCDHB12		PCDHB12	PCDHB12
	PCDHB13: protocadherin beta 13		PCDHB13: protocadherin beta 13	PCDHB13: protocadherin beta 13
	Pcdhb17		Pcdhb17	Pcdhb17

	PCDHB4		PCDHB4	PCDHB4
	PCDHGB1		PCDHGB1	PCDHGB1
	PCDHGB6		PCDHGB6	PCDHGB6
	Pen-2	Pen-2		
	PMPCB		PMPCB	
	PP2C gamma		PP2C gamma	
	Presenilin 1	Presenilin 1		
	Presenilin 2	Presenilin 2		
	Protocadherin 7		Protocadherin 7	Protocadherin 7
	Protocadherin beta 16		Protocadherin beta 16	Protocadherin beta 16
	Protocadherin beta 8		Protocadherin beta 8	Protocadherin beta 8
	RAB-18		RAB-18	
	Rab3 GTPase-activating protein, non-catalytic subunit		Rab3 GTPase-activating protein, non-catalytic subunit	
	Retinal short-chain dehydrogenase/reductase retSDR2		Retinal short-chain dehydrogenase/reductase retSDR2	Retinal short-chain dehydrogenase/reductase retSDR2
	RNASEL		RNASEL	
	Sideroflexin 1		Sideroflexin 1	
	Signal transducer and		Signal transducer and	

		activator of transcription-1		activator of transcription-1	
		Similar to CGI-135 protein		Similar to CGI-135 protein	Similar to CGI-135 protein
		SMAP-1B		SMAP-1B	
		SPTLC2		SPTLC2	
		Sterile alpha and HEAT/Armadillo motif protein		Sterile alpha and HEAT/Armadillo motif protein	Sterile alpha and HEAT/Armadillo motif protein
		Sterol O-acyltransferase 1		Sterol O-acyltransferase 1	
		STMN3		STMN3	
		tegt: testis enhanced gene transcript (bax inhibitor 1)		tegt: testis enhanced gene transcript (bax inhibitor 1)	tegt: testis enhanced gene transcript (bax inhibitor 1)
		Thioredoxin domain-containing protein		Thioredoxin domain-containing protein	Thioredoxin domain-containing protein
		Triple functional domain protein (PTPRF interacting)		Triple functional domain protein (PTPRF interacting)	
		UNC5C		UNC5C	

		Vacuolar ATP synthase membrane sector associated protein m8-9		Vacuolar ATP synthase membrane sector associated protein m8-9	Vacuolar ATP synthase membrane sector associated protein m8-9
		vacuolar protein sorting protein 18		vacuolar protein sorting protein 18	
		Y391_HUMAN		Y391_HUMAN	Y391_HUMAN
Pen-2- complex	Pen-2	Alpha-2 catenin		Alpha-2 catenin	
		Aph-1a	Aph-1a		
		COPINE FAMILY MEMBER.		COPINE FAMILY MEMBER.	COPINE FAMILY MEMBER.
		Copine III		Copine III	
		Dachshund 2		Dachshund 2	
		Delta-1 catenin		Delta-1 catenin	
		KIAA1102 (Fragment)		KIAA1102 (Fragment)	KIAA1102 (Fragment)
		MGC2803		MGC2803	MGC2803
		Nicastrin	Nicastrin		
		Pen-2	Pen-2		
		Presenilin 1	Presenilin 1		
		Presenilin 2		Presenilin 2	

		TNRC15		TNRC15	TNRC15
		TPST1		TPST1	
		ZIP kinase		ZIP kinase	
APP695SW-complex	APP695SW	APP695SW	APP695SW		
		Fe65	Fe65		
		Fe65L1	Fe65L1		
		FLJ10773		FLJ10773	FLJ10773
		GTF2I		GTF2I	
		IL13RA2		IL13RA2	
		Integral membrane protein 2B (ITM2B)		Integral membrane protein 2B (ITM2B)	
		Integral membrane transporter protein		Integral membrane transporter protein	
		JIP-1	JIP-1		
		S-100 alpha		S-100 alpha	
		X11beta	X11beta		
APP-C99-complex	APP-C99	APP		APP	
		APP-C99	APP-C99		
		CAMK2D		CAMK2D	
		Delta-like homolog		Delta-like homolog	

	Fe65	Fe65			
	Fe65L1	Fe65L1			
	Integral membrane transporter protein			Integral membrane transporter protein	
	KIAA1102 (Fragment)			KIAA1102 (Fragment)	KIAA1102 (Fragment)
	KIAA1949			KIAA1949	KIAA1949
	MGC4022			MGC4022	MGC4022
	MGC5442			MGC5442	MGC5442
	NAP-1 related protein			NAP-1 related protein	
	Neurocalcin delta			Neurocalcin delta	
	REST corepressor			REST corepressor	
	S-100 alpha			S-100 alpha	
	S-100 beta			S-100 beta	
	X11beta			X11beta	
Tau-complex	Tau	14-3-3 protein zeta/delta	14-3-3 protein zeta/delta		
		Actin	Actin		
		Alpha tubulin	Alpha tubulin		
		Beta tubulin	Beta tubulin		
		Deoxyhypusine synthase		Deoxyhypusine synthase	
		Dynactin 2		Dynactin 2	

	MEP50		MEP50	MEP50
	Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1		Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1	
	PPP2CA (PP2A, catalytic subunit, alpha)	PPP2CA (PP2A, catalytic subunit, alpha)		
	PPP2CB (PP2A, catalytic subunit, beta)	PPP2CB (PP2A, catalytic subunit, beta)		
	PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)	PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)		
	PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)	PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)		
	S-100 beta		S-100 beta	
	Tau	Tau		

TABLE 2

## INDIVIDUAL PROTEINS OF THE COMPLEXES

Protein name	SEQ ID	IPI number	Molecular weight
14-3-3 protein epsilon	1	IPI00000816.1	29174
14-3-3 protein beta/alpha	2	IPI00216318.1	28082
14-3-3 protein eta	3	IPI00216319.1	28219
14-3-3 protein gamma	4	IPI00220642.1	28303
14-3-3 protein tau	5	IPI00018146.1	27764
14-3-3 protein zeta/delta	6	IPI00021263.1	27745
18 kDa microsomal signal peptidase subunit	100	IPI00104128.1	20625
200 kDa proteasome activator	101	IPI00005260.1	206407
23 kDa microsomal signal peptidase	221	IPI00030262.2	20253
25 kDa microsomal signal peptidase subunit	185	IPI00014148.1	25003
ABCB11	102	IPI00030011.1	146393
ABCC1	222	IPI00008338.1	164941
Acetolactate synthase homolog	107	IPI00009963.2	67868
Actin	305	IPI00021439.1	41737
ADAMTS-19	25	IPI00152639.1	134062
Adrenoleukodystrophy protein	108	IPI00017637.1	82909
Alpha tubulin	306	IPI00142632.1	50152



Alpha-2 catenin	280	IP100030907.1	105282
Aph-1a	109	IP100059964.1	28996
APLP1	7	IP100020012.1	72176
APLP2	8	IP100031030.1	86956
APP	9	IP100006608.1	86943
APP695SW	290	CZB000000007.1	78630
APP-C99	10	CZB000000004.1	11277.9
ATM	103	IP100012732.1	350644
ATP1B1	223	IP100006484.1	35061
ATP2C1	224	IP100024344.1	100576
ATP7A	106	IP100028610.1	163335
ATP-binding cassette protein, sub-family B, member 1	104	IP100027481.1	141463
ATP-binding cassette, sub-family A member 3	186	IP100017800.1	191388
ATP-binding cassette, sub-family B, member 7	11	IP100023879.1	82641
ATP-dependent metalloprotease FtsH1 homolog	105	IP100045946.1	86503
Axonemal dynein heavy chain 8	26	IP100014845.4	516063
BACE1	187	IP100011518.1	55764
BAT1	27	IP100218291.1	53243
Beta tubulin	307	IP100142634.1	49671

BIG1	110	IP100002188.1	208709
Brain-specific GTP-binding protein	225	IP100103530.1	63543
BSCv protein (FRAGMENT)	188	IP100031131.1	46480
BTAF1	111	IP100024802.1	206887
C20orf11 (sim to a region of RANBPM)	28	IP100016634.1	26749
Cadherin EGF LAG seven-pass G-type receptor 2	30	IP100015346.1	317453
Calcium-binding protein P22	117	IP100218924.1	22456
Calsyntenin-1	31	IP100007257.1	109793
Calsyntenin-2	32	IP100005491.1	107020
Calsyntenin-3	33	IP100156997.1	106098
CAMK2D	297	IP100013787.1	56297
CAMK4	189	IP100002921.1	51926
Casein kinase II beta chain	190	IP100010865.1	24942
Cathepsin B	191	IP100013478.1	37808
Cation-chloride cotransporter-interacting protein	118	IP100024998.1	96171
CD97	112	IP100012052.1	91941
CDM_HUMAN	113	IP100019387.1	27860
CDW92	226	IP100005068.2	73296
Centromere/kinetochore protein ZW10 homolog	119	IP100011631.1	88829
Cerebral protein 10	120	IP100018730.1	52118

CGB0_HUMAN	29	IP100032827.1	14585
CGI-13	114	IP100008847.1	52917
CGI-51	115	IP100215921.1	57429
cholinergic receptor, nicotinic, alpha polypeptide 3	183	IP100007259.1	55637
Chondroitin sulfate proteoglycan 6	34	IP100023102.1	141542
CHRNA3	116	IP100027751.1	57310
Chromatin-specific transcription elongation factor FACT 140 kDa subunit	35	IP100026970.1	119914
CNTNAP1	227	IP100219249.1	164756
COPINE FAMILY MEMBER.	281	IP100173232.1	61891
Copine III	282	IP100024403.1	60131
DAAM1	121	IP100000705.1	124245
Dachshund 2	283	IP100065787.1	65323
DAPK1	122	IP100021250.1	160018
DC6 protein	36	IP100024620.1	11529
DCTN1	192	IP100011446.1	127404
Delta-1 catenin	284	IP100015202.1	104958
Delta-6 fatty acid desaturase	193	IP100003544.1	52259
Delta-like homolog	298	IP100009191.1	41143
Deoxyhypusine synthase	308	IP100026829.1	40971
Dihydrofolate reductase	229	IP100030357.1	28844
Dkfp586c1924	37	IP100031064.1	21527

DNM1	228	IP100012033.1	97407
DOCK3	123	IP100217985.1	233103
Down syndrome critical region protein 2	124	IP100030770.1	32854
Dynactin 2	309	IP100013802.2	44231
Dynein light chain 2A	38	IP100023551.1	10922
Dynein light chain-A	39	IP100007675.1	56627
ECP-51	12	IP100009104.1	51157
ECSIT	125	IP100106506.1	49148
ELAVL3	40	IP100031552.2	39547
Endocytic receptor Endo180	233	IP100005707.3	166655
ENG	230	IP100017567.1	70578
ENG00000168820 (hypothetical protein with p-loop)	41	IP100151716.2	30772
ENSG00000144840	194	IP100102897.1	26308
ensp000000297280 (hypothetical protein with p-loop)	184	IP100182852.1	130960
Eukaryotic translation initiation factor 4A, isoform	42	IP100025491.1	46154
EXT2	231	IP100004047.1	82255
EXTL3	232	IP100015135.1	104749
FACL1	126	IP100013161.1	78348
FACL3	195	IP1000031397.1	80346
FACL4	196	IP100029737.1	79188

Fe65		13	IP100010843.1	77244
Fe65L1		292	IP100023841.1	81080
Filamin, gamma		45	IP100165017.1	291151
FLJ10773		291	IP100171198.1	52401
FLJ13660		234	IP100100927.1	56921
FLJ13910		43	IP100009707.1	43993
FLJ13977		197	IP100025520.1	53482
FLJ20342		127	IP100015713.1	65084
FLJ20420		128	IP100015833.1	26152
FLJ20481		198	IP100016418.1	47655
FLJ22390		199	IP100009343.1	17098
FLJ22555		129	IP100103303.1	32545
FLJ22678		130	IP100217885.1	85495
FRAP1		44	IP100031410.1	288892
Galactosyl/galactosylxylosylprotein 3-beta-glucuronosyltransferase 3		131	IP100014931.1	37062
GAP-associated tyrosine phosphoprotein p62		14	IP100008575.1	48227
GPR49		235	IP100021131.1	99998
GTF2I		293	IP100054042.1	112416
GTP-binding protein ERA		46	IP100026512.1	49098
HADH2/ERAB (mitochondrial enzyme)		47	IP100017726.1	26923

HDAC2	48	IP100023289.1	55325
HERC2 protein	49	IP100005826.1	527472
HK2	236	IP100005103.1	102368
homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)	219	IP100063544.1	33834
HSPC154	50	IP100107156.1	28202
HSPC245	51	IP100107104.1	26057
HTRA2	132	IP100001663.1	48841
HU-K4	133	IP100163951.1	48771
HU-K4	133	IP100163951.1	48771
Hunc18a	54	IP100046057.1	68736
HYPOTHETICAL PROTEIN	237	IP100164098.1	31105
Hypothetical protein (Fragment)	238	IP100161721.1	94945
HYPOTHETICAL PROTEIN FLJ10618	52	IP100018766.1	34095
Hypothetical protein FLJ10795	55	IP100024779.1	138430
HYPOTHETICAL PROTEIN FLJ12599.	53	IP100182757.1	102917
Hypothetical protein FLJ14562	239	IP100161141.1	67283
Hypothetical protein FLJ20397	56	IP100101654.1	26305
Hypothetical protein FLJ23356	135	IP100031005.1	40050
Hypothetical protein FLJ23630	240	IP100103520.1	73732
Hypothetical protein KIAA0372	241	IP100005634.1	175486

Hypothetical protein KIAA0455	136	IPi00160410.1	82983
Hypothetical protein KIAA0971-I	137	IPi00013735.1	81463
hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5	275	IPi00012235.1	24899
hypothetical protein MGC13186	98	IPi00031570.1	20713
hypothetical protein MGC22916	276	IPi00172590.1	88020
HYPOTHEICAL PROTEIN XP_174405.	134	IPi00159547.1	23035
ICAM-2	200	IPi00009477.1	30653
IGF2R	242	IPi00007226.1	274309
IKAP	57	IPi00028877.1	150191
IL13RA2	294	IPi00032199.1	44176
Insulinoma-glucagonoma protein 20	58	IPi00103536.1	183267
Integral membrane protein 2B (ITM2B)	16	IPi00031821.1	30338
Integral membrane transporter protein	277	IPi00020093.1	31735
IPi00104084.1	15	IPi00104084.1	36759
ITPR1	243	IPi00036162.1	313945
JIP-1	295	IPi00023133.1	77524
KIAA0056	59	IPi00000899.1	169718
KIAA0062 (FRAGMENT)	138	IPi00014236.1	58417
KIAA0090	139	IPi00160376.1	111759

KIAA0095	201	IP100005680.1	93488
KIAA0103	140	IP100014149.1	34833
KIAA0166	60	IP100001458.1	250749
KIAA0251 (FRAGMENT)	244	IP100010861.1	90027
KIAA0325 (FRAGMENT)	61	IP100141330.2	532367
KIAA0363 (FRAGMENT)	245	IP100004538.1	156999
KIAA0564	62	IP100158296.2	214824
KIAA0763	63	IP100006669.1	94914
KIAA0922	202	IP100021671.1	138688
KIAA0971	246	IP100007231.1	74536
KIAA1102 (Fragment)	285	IP100160387.1	121739
KIAA1181 (FRAGMENT)	203	IP100003635.1	36879
KIAA1250	247	IP100033429.1	197211
KIAA1533 (FRAGMENT)	204	IP100001841.1	72964
KIAA1949	299	IP100150950.1	67959
Krab box protein ensp00000302970	17	IP100154267.1	37912
Laminin, gamma 1	65	IP100003398.1	177607
LIB ( leucine-rich repeat protein)	64	IP100057018.2	64414
LRP5	248	IP100024531.1	179173
MBIP	66	IP100009868.1	39236
MEGF7 (FRAGMENT)	67	IP100023954.2	175609
MEP50	310	IP100012202.1	36724



Mesenchymal stem cell protein DSCD75	205	IP100010292.1	23865
MGC2803	286	IP100031526.1	18419
MGC4022	300	IP100010625.1	59797
MGC4248	141	IP100031582.1	24274
MGC5442	142	IP100027773.1	26261
MT-ACT48	68	IP100032410.1	46355
Myosin IXB	69	IP100003064.1	228624
NAP-1 related protein	301	IP100155244.1	44159
NEU1	70	IP100029817.1	45467
Neurexin-1	73	IP100006314.1	161883
Neurocalcin delta	302	IP100149712.1	22114
Neurotrypsin	206	IP100011063.1	97012
Nicastrin	147	IP100021983.1	78411
NICE-3	143	IP100032413.1	28779
NIPSNAP1	71	IP100021086.2	33310
NIPSNAP2	72	IP100016077.1	33743
NPC1	144	IP100005107.1	142149
NPD002	145	IP100152981.1	68760
NPL4, a component of the nuclear pore complex	146	IP100001676.1	73788
NRP2	249	IP100029693.1	104831

Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1	311	IP100002922.2	55595
P63 protein	148	IP100141318.1	66022
Paladin	77	IP100161782.1	96754
PAS domain containing serine/threonine kinase	207	IP100141040.1	142859
PCDHA10	250	IP100001513.1	102875
PCDHB12	251	IP100001450.1	86770
PCDHB13: protocadherin beta 13	252	IP100001449.1	87552
Pcdhb17	258	IP100045942.1	64852
PCDHB4	253	IP100001429.1	87270
PCDHGB1	254	IP100003890.1	100360
PCDHGB6	255	IP100003897.1	101043
PDZ and LIM domain protein 1	74	IP100010414.2	36072
PDZ domain protein MAGI-3	18	IP100022491.1	111914
Pen-2	209	IP100020516.1	12029
Phosphoenolpyruvate carboxykinase 2 (mitochondrial)	78	IP100004383.1	70637
PILB	75	IP100032871.1	21468
PILT	76	IP100010544.2	60705
PMPCB	256	IP100025726.1	54168
PP1, regulatory subunit 15B	208	IP100045837.1	79125
PP2C gamma	257	IP100006167.1	59272

PPP2CA (PP2A, catalytic subunit, alpha)	312	IP100008380.1	35594
PPP2CB (PP2A, catalytic subunit, beta)	313	IP100003461.1	35575
PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)	314	IP100025326.1	65092
PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)	19	IP100220836.1	55642
Presenilin-1	210	IP100026333.1	52163
Presenilin-2	172	IP100028485.1	50140
Procollagen C-endopeptidase enhancer	79	IP100014828.1	47972
Programmed cell death 10	80	IP100026997.1	24658
Prohibitin	173	IP100017334.1	29804
Protein amplified in osteosarcoma (OS-9)	211	IP100013268.1	75562
Protein similar to AGCP6688	81	IP100140709.1	14290
Protein similar to probable mitotic centromere associated kinesin	20	IP100088667.1	18400
Protein similar to stromal cell-derived factor 2	212	IP100034198.1	23026
Protocadherin 7	259	IP100001893.2	116105
Protocadherin beta 16	260	IP100016595.1	84936
Protocadherin beta 8	213	IP100009033.1	87624
PSMA1	149	IP100016832.1	29556
PSMA3	150	IP100016834.1	28302

PSMA4	151	IP100016836.1	29484
PSMA6	152	IP100029623.1	27399
PSMB1	153	IP100025019.1	26489
PSMB2	154	IP100028006.1	22836
PSMB3	155	IP100028004.2	22949
PSMB4	156	IP100000806.1	29192
PSMB5	157	IP100219629.1	28480
PSMB6	158	IP100000811.2	25358
PSMC1	159	IP100011126.2	49185
PSMC2	160	IP100021435.1	48634
PSMC3	161	IP100018398.2	49204
PSMC4	162	IP100020042.2	47366
PSMC5	163	IP100023919.2	45626
PSMC6	164	IP100021926.2	44173
PSMD1	165	IP100015333.1	105866
PSMD11	166	IP100105598.1	47464
PSMD12	167	IP100003569.1	52904
PSMD13	168	IP100003570.1	42945
PSMD2	169	IP100012268.1	100200
PSMD3	170	IP100011603.2	60978
PSMD4	171	IP100022694.1	40737
RAB-18	261	IP100014577.1	22977

Rab3 GTPase-activating protein, non-catalytic subunit	263	IP100018280.3	155985
RAB7L1	82	IP100024775.1	23155
RANBP1	83	IP100018856.1	23310
Reelin	85	IP100021018.1	388402
REP8 protein	214	IP100010353.1	30541
REST corepressor	303	IP100008531.1	53028
Retinal short-chain dehydrogenase/reductase retSDR2	216	IP100008260.1	32964
RING finger protein 5	215	IP100012608.1	19881
RNASEL	262	IP100015864.1	83533
RNB6	21	IP100008862.1	44792
RPGR-interacting protein 1	84	IP100044777.1	103123
RPS6KA3	174	IP100020898.1	83736
S-100 alpha	296	IP100010824.1	10415
S-100 beta	304	IP100220413.1	10713
SAP-62	22	IP100017341.2	49256
Serine/threonine protein phosphatase 6	90	IP100012970.1	35144
Sideroflexin 1	266	IP100009368.2	35619
Signal transducer and activator of transcription-1	267	IP100030781.1	87335
Similar to CGI-135 protein	268	IP100007052.1	16980

SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10.		175	IP100058185.3	95055
similar to SD27354p [ <i>Drosophila melanogaster</i> ]		99	IP100103057.1	13291
SMAP-1B		264	IP100072534.1	103077
SNAP-25		86	IP100010470.1	23315
Sortilin 1		177	IP100016022.1	92100
Sortilin-related receptor		91	IP100022608.1	248441
SPTLC2		265	IP100005751.1	62924
Stearoyl-CoA desaturase		178	IP100100476.1	41523
Sterile alpha and HEAT/Armadillo motif protein		269	IP100007919.1	75337
Sterol O-acyltransferase 1		270	IP100019898.1	64763
STMN3		87	IP100021199.2	21017
STRA6 isoform 1		176	IP100154566.1	73533
Stromal cell-derived factor 2-like 1		217	IP100106642.2	23511
STX1A		88	IP100003370.1	33023
SUCLA2		89	IP100021996.2	50331
Synaptogyrin 3		92	IP100013947.1	24555
Tau		315	IP100025499.1	45850
tegt: testis enhanced gene transcript (bax inhibitor 1)		278	IP100022748.2	26538
Thioredoxin domain-containing protein		218	IP100001028.1	32535

TNRC15	287	IP100160501.1	127290
Tparl	179	IP100102213.1	34906
TPST1	288	IP100030106.1	42188
Transcription factor CP2	23	IP100037599.1	57256
Triple functional domain protein (PTPRF interacting)	271	IP100026676.1	324106
TYK2	93	IP100022353.1	133660
tyrosine phosphatase ensg00000149185	220	IP100102935.1	22844
Ubiquitin-protein ligase E3-alpha	94	IP100156938.1	83595
Ubiquitin-protein ligase EDD	180	IP100026320.1	309352
UNC5C	272	IP100021472.1	103102
Vacuolar ATP synthase membrane sector associated protein m8-9	273	IP100041030.1	39036
vacuolar protein sorting protein 18	279	IP100060946.1	64959
VGF nerve growth factor inducible protein	95	IP100019628.1	67287
Voltage-dependent anion channel 2	181	IP100019625.1	31595
Wolframin	182	IP100008711.1	100306
X11beta	96	IP100017817.1	82512
X11beta	96	IP100017817.1	82512
Y391_HUMAN	274	IP100004584.1	65486
Zinc finger protein 198	97	IP100032608.2	154911
Zinc finger protein 277	24	IP100220069.1	56818

ZIP kinase	289	IPI00015213.1	52536
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TABLE 3

## BIOCHEMICAL ACTIVITIES OF THE COMPLEXES

Name of Complex	Biochemical activity
Fe65-complex	Regulator of APP processing and APP function
X11beta-complex	Regulator of APP processing and APP function
PSEN2-complex	Gamma-secretase complex
Nicastrin-complex	Gamma-secretase activity and assembly (trafficking)
Aph-1a-complex	Gamma-secretase activity and assembly (trafficking)
Pen-2-complex	Gamma-secretase activity and assembly (trafficking)
APP695SW-complex	Signalling activity (regulator of transcription)
APP-C99-complex	Signalling activity (regulator of transcription)
Tau-complex	Regulator of microtubules and vesicle transport along microtubules
APP695SW	Signalling activity (regulator of transcription)

TABLE 4

## MEDICAL APPLICATIONS OF THE COMPLEXES

Complex	Medical application
Fe65-complex	neurodegenerative disease such as Alzheimer's disease; inflammatory diseases such as chronic inflammatory disorders, rheumatoid arthritis and inflammatory bowel disease; cancer such as prostate cancer and breast cancer and skin cancer
X11b-complex	neurodegenerative disease such as Alzheimer's disease; inflammatory conditions such as ulcerative colitis, Crohn's disease and arterosclerosis
PSEN2-complex	neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders
Nicastrin-complex	neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders
Aph-1a-complex	neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders
Pen-2-complex	neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders
APP695SW-complex	neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders
APP-C99-complex	neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders
Tau-complex	neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders

The present invention is not to be limited in scope by the specific embodiments described herein. Indeed, various modifications of the invention in addition to those described herein will become apparent to those skilled in the art from the foregoing description and accompanying figures. Such modifications are intended to fall within the scope of the appended claims.

Various publications are cited herein, the disclosures of which are incorporated by reference in their entireties.

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29. Jan. 2004

**CLAIMS**

1. A protein complex selected from complex (I) and comprising
  - (a) at least one first protein, which first protein is selected from the group of proteins in table 1, fourth column of a given complex, or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of said protein, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid encoding said protein under low stringency conditions; and
  - (b) at least one second protein, which second protein is selected from the group of proteins in table 1, fifth column of said given complex, or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of said second protein, said variant being encoded by a nucleic acid that hybridizes to the nucleic acid encoding said protein under low stringency conditions; and a complex (II) comprising at least two of said second proteins,wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4) 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.
2. A protein complex comprising a first protein selected from the proteins listed in table 1, fourth column of a given complex or a homologue or variant thereof, or a functionally active fragment or functionally active derivative of said first protein, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid of said first protein under low stringency conditions, and at least one second protein selected from the group of proteins in table 1, fifth column of a given complex, or a variant or homologue thereof, or a functionally active fragment or a functionally active derivative of said second protein, the variant of said second protein being encoded by a nucleic acid that hybridizes to the nucleic acid of said second protein under low-stringency conditions, and wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% BSA, 100 ug/ml denatured salmon sperm

DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4) 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.

3. A protein complex comprising all proteins selected from the proteins in table 1, third column of a given complex or at least one protein being a homologue thereof, or a variant thereof or functionally active fragment or functionally active derivative of said protein, said variant being encoded by a nucleic acid that hybridizes to the nucleic acid of said protein under low stringency conditions;  
wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.
  
4. A protein complex that comprises all proteins as listed in table 1, third column for a given complex or at least one protein being a homologue or a variant thereof, or a functionally active fragment or a functionally active derivative thereof, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid of any of said proteins under low stringency conditions, except at least one protein of the proteins listed in table 5, third column, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C, with the proviso that the complex comprises at least one protein selected from table 1, fifth column of a given complex.

5. The complex of any of Claim 1 - 4 comprising at least one functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein.
6. The complex of Claim 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.
7. The complex of any of Claim 1 - 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.
8. The complex of any of Claim 1 - 7 that is involved in at least one biochemical activity as stated in table 3.
9. A process for preparing a complex of any of Claim 1 - 8 and optionally the components thereof comprising the following steps:  
expressing a protein of the complex, preferably a tagged protein, in a target cell, or a tissue or an organ, isolating the protein complex which is attached to the protein, preferably the tagged protein, and optionally disassociating the protein complex and isolating the individual complex members.
10. The process according to Claim 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.
11. The process according to any of Claim 9 - 10 wherein the two tags are separated by a cleavage site for a protease.
12. Component of a protein complex obtainable by a process according to any of Claim 9 - 11.
13. Protein selected from the group of proteins in table 1, sixth column of a given complex or a homologue or a variant of thereof, or a functionally active fragment or a

functionally active derivative of said protein, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid encoding said protein under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.

14. Nucleic acid encoding a protein according to Claim 13.
15. Construct, preferably a vector construct, comprising
  - (a) a nucleic acid according to Claim 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or
  - (b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative thereof, or a homologue or a variant thereof, at least one of said proteins being selected from the first group of proteins according to Claim 1 (a) and at least one of said proteins, being selected from the second group of proteins according to Claim 1 (b) or
  - (c) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative thereof, or a homologue or a variant thereof, said proteins being selected from the proteins of complex (II) according to Claim 1.
16. Host cell, containing a vector comprising at least one nucleic acid of Claim 14 and /or a construct of Claim 15 or containing several vectors each comprising at least one nucleic acid encoding at least one protein selected from the first group of proteins according to Claim 1 (a) and at least one nucleic acid encoding at least one protein selected from the second group of proteins according to Claim 1 (b).
17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of

Claim 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody containing the binding domain thereof which binds to any of the proteins of the group of proteins according to Claim 13.

18. A kit comprising in one or more containers:

- (a) the complex of any of Claim 1 – 8 and/or the proteins of Claim 13 and/or
- (b) an antibody according to Claim 17 and/or
- (c) a nucleic acid encoding a protein of the complex of any of Claim 1 – 8 and/or a protein of Claim 13 and/or
- (d) cells expressing the complex of any of Claim 1 – 8 and/or a protein of Claim 13 and, optionally,
- (e) further components such as reagents, buffers and working instructions.

19. The kit according to Claim 18 for processing a substrate of a complex of any one of Claim 1 - 8.

20. The kit according to Claim 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as those as stated in column 2, table 4 of a given complex.

21. Array, preferably a microarray, in which at least a complex according to any of Claim 1 - 8 and/or at least one protein according to Claim 13 and/or at least one antibody according to Claim 17 is attached to a solid carrier.

22. A process for modifying a substrate of a complex of any one of Claim 1 - 8 comprising the step of bringing into contact a complex of any of Claim 1 - 8 with said substrate, such that said substrate is modified.

23. A pharmaceutical composition comprising the protein complex of any of Claim 1 - 8 and/or a protein according to Claim 13.

24. A pharmaceutical composition according to Claim 23 for the treatment of diseases and disorders, preferentially for diseases or disorders such as those as stated in column 2, table 4 of a given complex.
25. A method for screening for a molecule that binds to a complex of any one of Claim 1 - 8 and/or a protein of Claim 13, comprising the following steps:
- (a) exposing said complex or protein, or a cell or organism containing said complex or said protein, to one or more candidate molecules; and
  - (b) determining whether said candidate molecule is bound to the complex or protein.
26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of a complex of any one of Claim 1 - 8 comprising the steps of:
- (a) exposing said complex, or a cell or organism containing said complex to one or more candidate molecules; and
  - (b) determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene regulated by the complex and/or the abundance and/or activity of a protein or protein complex dependent upon the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene regulated by the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity, or composition of said complex.
27. The method of Claim 26, wherein the amount of said complex is determined.
28. The method of Claim 26, wherein the activity of said complex is determined.

29. The method of Claim 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.
30. The method of Claim 26, wherein the amount of the individual protein components of said complex is determined.
31. The method of Claim 30, wherein said determining step comprises determining whether any of the proteins listed in table 1, third column of said complex, or a functionally active fragment or a functionally active derivative thereof, or a variant or a homologue thereof, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid of said protein under low-stringency conditions, is present in the complex.
32. The method of any of Claim 26 - 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder, preferentially of a disease or disorder selected from the diseases or disorders such as those as stated in column 2, table 4 of a given complex.
33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of Claim 1 - 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder, preferentially of a disease or disorder such as those as stated in column 2, table 4 of a given complex.
34. A method for the production of a pharmaceutical composition comprising carrying out the method of Claim 26 - 31 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.

35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, component disposition of, or intracellular localization of the complex of any one of the Claim 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene regulated by the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in a corresponding sample from a subject not having the disease or disorder or predisposition indicated the presence in the subject of the disease or disorder or predisposition in the subject.
36. The method of Claim 35, wherein the amount of said complex is determined.
37. The method of Claim 35, wherein the activity of said complex is determined.
38. The method of Claim 37, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.
39. The method of Claim 35, wherein the amount of the individual protein components of said complex is determined.
40. The method of Claim 39, wherein said determining step comprises determining whether any of the proteins according to Claim 13 is present in the complex.
41. The complex of any one of Claim 1 - 8, or a protein of Claim 13 or an antibody or fragment thereof of Claim 17, for use in a method of diagnosing a disease or disorder, preferentially of a disease or disorder such as neurodegenerative disease such as those as stated in column 2, table 4 of a given complex.



42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity of, component composition of or intracellular localization of, the complex of any one of Claim 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, activity of, or protein composition of, said complex.
43. The method according to Claim 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.
44. The method according to Claim 42, wherein said disease or disorder involves increased levels of the amount or activity of said complex.
45. Complex of Claim 1 - 8 and/or a protein as listed in table 1, fifth column of said complex as a target for an active agent of a pharmaceutical, preferably a drug target, in the treatment or prevention of a disease or disorder, preferentially of a disease or disorder such as a neurodegenerative disease such as those as stated in column 2, table 4 of a given complex.

29. Jan. 2004

**SEQUENCES****SEQID No:1**

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**SEQID No:2**

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 AKLRRVQRPEDASGGSSPSGTSKSDANRASSGGGGGGLMEEMNKLLAKRRKAASQS  
 DKPAEKKEDESQMEDPSTSPSPGTRAASQPPNSSEAGRKPWERSNSVEKPVSSILSRT  
 PSVAKSPEAKSPLQSQPHSRMKPAGSVNDMALDAFDLDRMKQEILEEVVRELHKVKEE  
 IIDAIRQELSGISTT

## SEQID No:22

MDFQHRPGGKTGSGGVASSSESNRDRRERLRQLALETIDINKDPYFMKNHLGSYECKL  
 CLTLHNNEGSYLAHTQGKKHQTNLARRAAKEAKEAPAQPAPEKVKVEVKKFKVIGRPG  
 YKVTKQRDSEMGQQSLLFQIDYPEIAEGIMPRHRFMSAYEQRIEPPDRRWQYLLMAAE  
 PYETIAFKVPSREIDKAEGKFWTHWNRETQFFLQFHFMEKPPAPPSLPAGPPGVKR  
 PPPPLMNGLPPRPPLPESLPPPPPGGLPLPMPPTGPAPSGPPGPPQLPPPAPGVHPP  
 APVVHPPASGVHPPAPGVHPPAPGVHPPAPGVHPPTSGVHPPAPGVHPPAPGVHPPA  
 PGVHPPAPGVHPPAPGVHPPPSAGVHPQAPGVHPPAAPAVHPQAPGVHPPAPGMHPQ  
 APGVHPQPPGVHPSAPGVHPQPPGVHPSNPGVHPPTMPMPMLRPPLPSEGPGNIPPP  
 PPTN

## SEQID No:23

MAWALKLPLADEVIESGLVQDFDASLSGIGQELGAGAYSMSDVLALPIFKQEESLPPD  
 NENKILPFQYVLCAATSPAVKLHDETLTYLNQGQSYEIRMLDNRKLGELPEINGKLVKSIF  
 RVVFHDRRLQYTEHQQLEGWRWNRPGDRILDIDIPMSVGIIDPRANPTQLNTVEFLWDP  
 AKRTSVFIQVHCISTEFTMRKHGGEKGVPRVQIDTFKENENGEYTEHLHSASCQIKVFK  
 PKGADRKQKTDREKMEKRTPEHEKEYQPSYETITLTCSPWPETIYVNNSPSPGFNSS  
 HSSFSLGEGNGSPNHQPEPPPPVTDNLLPTTTPQEAQQWLHRNRFFSTFTRLFTNFSGA  
 DLLKLTRDDVIQICGPADGIRLFNALKGRMVRPRLTIYVCQESLQLREQQQQQQQQQQK  
 HEDGDSNGTFFVYHAIYLEELTAVELTEKIAQLFSISPCQISQIYKQGPTGIHVLISDEMIQ  
 NFQEEACFILDTMKAETNDSYHIILK

## SEQID No:24

VWRKHYYVDGEFASSSVSTGATPPPTRPAALPFLFCRVMAASKTQGAVARMQEDRDGS



CSTVGGVGYGDSKDCILEPLSLPESPGGTTTLEGSPSVPCIFCEEHFPVAEQDKLLKHM  
 IEHKIVIADVCLVADFQRYILYWRKRFT EQPITDFCSVIRINSTAPFEEQENYFLLCDVLPE  
 DRILREELQKQRLREILEQQQQERNDTNFHGVCMFCNEEFLGNRSVILNHMAREHAFNI  
 GLPDNIVNCNEFLCTLQKKLDNLQCLYCEKTFRDKNTLKDHRKKQHRKINPKNREYDR  
 FYVINYLELGKSWEEVQLEDDRELLDHQEDDWSDEEHPASAVCLFCEKQAETIEKLY  
 VHMEDAHEFDLLKIKSELGLNFYQQVKLVNFIRRVHQCRCYGVCHVKFKSKADLRTHM  
 EETKHTSLLPDRKTWDQLEYFYPTYENDTLLCTLSDSESDLTAEQENENVPIISEDTSKL  
 YALKQSSILNQLLL

SEQID No:25

MRLTHICCCCLLYQLGFLSNGIVSELQFAPDREEWEVVPALWRREPVDPAAGGSGGSA  
 DPGWVRGVGGGGGSARAQAAGSSREVRVAPVPLEEPVEGRSESRLRPPPPSEGEED  
 EELESQELPRGSSGAAALSPGAPASWQPPPPPPQPPSPPPAQHAEPDGDEVLLRIPAF  
 SRDLYLLLRRDGRFLAPRFAVEQRPNP GPGPTGAASAPQPPAPPDAGCFYTGAVLRHP  
 GSLASFSTCGGGLMGFIQLNEDFIFIEPLNDTMAITGHPHRVYRQKRSMEEKVTEKSAL  
 HSHYCGIISDKGRPRSRKIAESGRGKRYSYKLPQEYNIETVVVADPAMVSYHGADAARR  
 FILTILNMVFNLFQHKSLGVQVNLRVIKLILLHETPPELYIGHHGEKMLESFCKWQHEEFG  
 KKNDIHLEMSTNWGEDMTSVDAAILITRKDFCVHKDEPCDTVGIAYLSGMCSEKRKCIIA  
 EDNGLNLAFTIAHEMGMHNMGINHDNDHPSCADGLHIMSGEWIKGQNLGDVSWSRCSK  
 EDLERFLRSKASNCLLQTNPQSVNSVMVPSKLPGMTYTADEQCQILFGPLASFQEMQ  
 HVICTGLWCKVEGEKECRTKLDPMDGTDCDLGKWCKAGECTSR TSAPEHLAGEWSL  
 WSPCSRTCSAGISSRERKCPGLDSEARDCNGPRKQYRICENPPCPAGLPGFRDWQCQ  
 AYSVRTSSPKHILQWQAVLDEEKPCALFCSPVGKEQPILLSEKVM DGTSCGYQGLDICA  
 NGRCQKVGCDGLLGLSLAREDHCGVCNGNGKSKIIKGDFNHTRGAGYVEVLVIPAGAR  
 RIKVVEEKPAHSYLALRDAGKQSINSDWKIEHSGAFNLAGTTVHYVRRGLWEKISAKGP  
 TTAPLHLLVLLFQDQNYGLHYEYTIPSDPLPENQSSKAPEPLFMWHTSWEDCDATCG  
 GGERKTTVSCTKIMSKNISIVDNEKCKYLTKPEPQIRK CNEQPCQTRWMMTEWTPCSR  
 TCGKGMQSRQVACTQQLSNGTLIRARERDCIGPKPASAQRCEGQDCMTVWEAGVWS  
 EFSVKCGKGIRHRTVRCTNPRKKCVLSTRPREAEDCEDYSKCYVWRMGDWSKCSITC  
 GKGMQSRVIQCMHKITGRHGNECFSSSEKPAAYR PCHLQPCNEKINVNTITSPRLAALTF  
 KCLGDQWPVYCRVIREKNLCQDMRWYQRCCECTCRDFYAQKLQQKS

SEQID No:26

MMKLYIDNAAPDKLKGLCIEFFVRCRNDVAINVKTIQEEALFTVLDASKGLLNGIRDMLANI

FLPAVLATNNWGALNQSKQGESEKHIFTETINRYLSFLDGARISIEGTVKLKTIDNVNFSK  
 LHTFEEVTAASNSSETVHQLEEVLMVWYKQIEQVLIIESEQMRKEAGDSGPLTELEHWK  
 RMSAKFNYIIEQIKGPSCKAVINVLNVAHSLKLLKNWRDLARITDTANESKDNVRYLYTLE  
 KVCQPLYNHDLVSMAGIQNLINAIIRMIHGVSRYYNTSERMTSLFIKVTNQMVTACKAYI  
 TDGGLNHVWDQETPVVLKKIQDCIFLKEYQASFHKTRKLISESSGEKSFEVSEMYIFGK  
 FEAFCRLEKITEMITVVQTYSTLSNSTIEGIDIMAIKFRNIYQGVKKKQYDILDPRRTEFD  
 TDFLDFMTKINGLEVQIQAFMNSSFGKILSSQQALQLLQRFQKLNIPCLGLEINHIERILQ  
 YYVAELDATKKASLYHSQKDDPPLARNMPPIAGKILWVRQLYRRISEPINYFFKNSDILSS  
 PDGKAVIRQYNKISYVLVEFEVYHTAWIREISQLHYALQATLFVRHPETGKLLVNFDPKI  
 LEVVRETKCMIKMKLDVPEQAKRLLKLESKLLKADKLYLQGLLQYYDELCOEVPSVFNL  
 MTPKMKKVESVLRQGLTVLTWSSLTLESFFQEVELVDMFNQLLKKISDLCEMHIDTVLK  
 EIAKTVLISLPESGATKVEDMLTLNETYTKEWADILNHKSKHVEEAVRELISIFEQIYEVKY  
 TGKVGKQSEQRKHVVFGSETGEGENNDYEANIVNEFDTHDKEDEFKKECKEVFAFFSH  
 QLLDSLQKATRLSLDTMKRRIFVARQVENMLIILYGRKQSEDIISFIKSEVHLAIPNVVMIP  
 SLDDIQQAINRMIQLTLEVSRGVAHWGQQQIRPIKSVIPSPTTTDVTHQNTGKLLKKEER  
 SFEEAIPARKLKNFYPGVAEHKDISKLVLSSSVNSLRKAAHEALQDFQKYKTLWTEDR  
 DVKVKEFLANNPSLTEIRSEILHYATFEQEIDELKPIIVVGALELHTEPMKLALSIEAKAWK  
 MLLCRYLNEEYKKKMSYMIAFINEYLKKLSRPIRDLDDVRFAMEALSCIRDNEIQMDMTL  
 GPIEEAYAILNRFEVEVTKEESEAVDTLRYSFNKLQSKAVSVQEDLVQVQPKFKSNLLES  
 VEVFREDVINFAEAYELEGPMPVNPQPQEQASNRLQIFQASFDLWRKFVTYSSGEQLFG  
 LPVTDYEVVHKTRKELNLLQKLYGLYDTVMSSISGYEILWGDVDIEKINAELLEFNRC  
 RKLPKGLKDWQAFLDLKKRIDDFSESCPLLEMMTNKAMKQRHWDRISELTGTPFDVES  
 DSFCLRNIMEAPLLKHKDDIEDICISAIKEKDIEAKLTQVIENWTNQNL SFAAFKKGKELL  
 KGTESGEIITLMEDSLMVLGSLLSNRYNAPFKKNIQNWVYKLSTSSDIIEEWLVVQNLWV  
 YLEAVFVGGDIKQLPQEAQRFNIDKSWIKIMQRAHENPNVINCCVGDETMGQLLPHL  
 HEQLEVCQKSLTGYLEKKRLLFPRFFFVSDPVILLEILGQASDSHTIQPHLPAVSDNINEVT  
 FhakdyDRIMAVISREGEKIVLDNSVMAKGPVEIWLLDLLKMQMSSLHNIIRSAFYQISDS  
 GFQLLPFLSHFPAQVGLLGIQMLWTHDSEEALRNAKDDRKIMQVTNQKFLDILNTLISQT  
 THDLSKFDRVKFETLITIHVHQRDIFDDL VKMHIKSPTDFEWLQKSRFYFKEDLDQTVVSI  
 TDVDFIYQNEFLGCTDRLVITPLTDRCYITLAQALGMNMGGAPAGPAGTGKTETTKDMG  
 RCLGKYVVVFNCSDQMDFRGLGRIFKGKCLAQSGSWGCFDEFNRIELPVLSVAAQQIYI  
 VLTARKERKKQFIFSDGDCVDLNPEFGIFLTMPGYAGRQELPENLKIQFRTVAMMVPD  
 RQIIMRVKLASCGFLENVILAQKFYVLYKLCEEQLTKQVHYDFGLRNILSVLRTLGSQKRA  
 RPEDSELSIVMRGLRDMNLSKLVDEDEPLFSLINDLFPGLQLDSNTYAELQNAVAHQV

QIEGLINHPPWNLKLVQLYETSLVRHGLMTLGPSGSGKTTVITILMKAQTECGRPHREM  
 RMNPKAITAPQMFGRLDTATNDWTDGIFSTLWRKTLKAKKGENIFLILDGPVDAIWENL  
 NSVLDDNKTLTLANGDRIPMAPSCKLLFEVHNIENASPATVSRMGMVYISSSALSWRPIL  
 QAWLKKRTAQEA AVFLTYEKFVEDTYTYMKLNLNPKMQLLECNYIVQSLNLLEGLIPSK  
 EEGGVSCVEHLHKLFVFGMLWSLGALLELESREKLEAFLRQHESKLDLPEIPKGSNQTM  
 YEFYVTDYGDWEHWNKKLQPYYYPTDSIPEYSSILVPNVNIRTNFLIDTIAKQHKAVLLT  
 GEQGTAKTVMVKAYLKKYDPEVQLSKSLNFSSATEPMMFQRTIESYVDKRIGSTYGPP  
 GGRKMTVFIDDINMPVINNEWGDQITNEIVRQMMEMEGMYSLDKPGDFTTIVDVQLIAAMI  
 HPGGGRNDIPQRLKRQFTVFNCTLPSNASIDKIFGIIGCGYFDPCRSFKPQICEMIVNLVS  
 VGRVLWQWTKVKMLPTPSKFHYIFNLRDLSRIWQGMLTIKAEECASIPTLLSLFKHECSR  
 VIADRFITPEDEQWFNAHLTRAveenIGSDAASCILPEPYFVDFLREMPEPTGDEPEDSV  
 FEVPKIYELMPSFDFLAEKLQFYQRQFNEIIRGTSLDLVFFKDAMTHLIKISRIIRTSCGNA  
 LLVGVGGSGKQSLSRLASFIAGYQIFQITLRSYNVTNLTDLALYKVAGADGKGITFIF  
 TDSEIKDEAFLEYLNNLLSSGEISNLFARDEMDEITQGLISVMKRELPRHPPTFDNLYEYF  
 ISRSRKNLHVLCFSPVGEKFRARSLKFPGLISGCTMDWFSRWPREALIAVASYFLSDY  
 NIVCSSEIKRQVVETMGLFHD MVSESCESYFQRYRRRAHVTPKSYLSFINGYKNIYAEK  
 VKFINEQAERMNIGLDKLMEASESVAKLSQDLAVKEKELAVASIKADEVLAEVTVSAQAS  
 AKIKNEVQEVKDKAQKIVDEIDSEKVKAESKLEAAKPALEEAEEAALNTIKPNDIATVRKLA  
 KPPHLIMRIMDCVLLL FQKKIDPVTMDPEKSCCKPSWGESLKLMSATGFLWSLQQFPKD  
 TINEETVELLQPYFNMDDYTFESA KKVCGNVAGLLSWTLAMAIFYGINREVLPLKANLAK  
 QEGR LAVANAELGKAQALLDEKQAELDKVQAKFDAAMNEKMDLLNDADTCRKKMQAA  
 STLIDGLSGEKIRWTQQSKEFKAQINRLVGDILLCTGFLSYLGPFNQIFRNYLLKDQWEM  
 ELRARKIPFTENLNLISMLVDPPTIGEWGLQGLPGDDLSIQNGIIVTKATRYPLLIDPQTQG  
 KTWIKSKEKENDLQVTSLNH KYFRTHLEDSSLGRPLIEDIHEELDPALDNVLEKNFIKS  
 GTTFKVKGDKCEDIMDTFKLYITTKLPNPAFTPEINAKTSVIDFTVTMKGLENQLLRRVIL  
 TEKQELEAERVKLLLEDVTFNKRKMKELEDNLLYKLSATKGS LVDDESLIGVLRTTKQTAA  
 EVSEKLHVA AE TEIKINAAQEEFRPAATRGSILYFLITEMSMVNIMYQTS LAQFLKLF DQS  
 MARSEK SPLPQKRITNII EYLT YE VFTYSVRGLYENHKFLFVLLMTLKIDLQRGT VKHREF  
 QALIKGGAALDLKACPPKPYRWILDMTWLNLVELSKLPQFAEIMNQISRNEKGWKS WFD  
 KDAPEEEIIPDGYNDSLDTCHKLLLIRSWCPDRTVFQARKYIADSLEEKYTEPVILNLEKT  
 WEESDTRTPLICFLSMGSDPTNQIDALAKKLECRTISMGGQGEVHARKLIQMSMQQ  
 GGWVLLQNCHLGLEFMEELETITTEASDDSF RVWITTEPHDRFPITLLQTS LKFTNEP  
 PQGVRAGLKRTFAGINQDLLDISNLP MWKPMLYTVAF LHSTVQERRKFGPLGWNIPYEF  
 NSADFSASVQFIQNH LDEC DIKGVSWNTVRYMIGEVQYGGRVTD DFDKRLNCFARV

WFSEKMFEPSFCFYTGKIPLCKTLDQYFEYIQSLPSLDNPEVFGLHPNADITYQSNTAS  
 AVLETITNIQPKESGGGVGETREAIVYRLSEDMLSKLPPDYIPHEVKSRLIKMGHLNSMNI  
 FLRQEIDRMQRVISILRSSLSDLKLAIEGTIIMSENLRDALDNMYDARIPQLWKRVSWDSS  
 TLGFWFTELLERNAQFSTWIFEGRPNVFWMTGFFNPQGFLTAMRQEVTRAHKGWALD  
 TVTIHNEVLRQTKEEITSPPGEGVYIYGLYMDGAAWDRRNGKLMESTPKVLFTQLPVLHI  
 FAINSTAPKDPKLYVCPIYKKPRRTDLTFITVVYLRTVLSPDHWILRGVALLCDIK

#### SEQID No:27

YLCFPLLFLNPLLFTPCFHLFCENPSRSPFPSSPAGPVMAENDVDNELLDYEDDEVETA  
 AGGDGAEAPAKKDVKGSYVSIHSSGFRDFLLKPELLRAIVDCGFEHPSEVQHECIPQAIL  
 GMDVLCQAKSGMGKTAVFVLATLQQLEPVTGQVSVLVMCHTRELAFQISKEYERFSKY  
 MPNVKVAVFFGGLSIKKDEEVLKKNCPHIVVGTPGRILALARNKSLNLKHIKHFILDECDK  
 MLEQLDMRRDVQEIFRMTPEHKQVMMFSAATLSKEIRPVCRKFMQDPMEIFVDDDETCLT  
 LHGLQQYYVKLKDNEKNRKLFDLLDVLEFNQVVIFVKSQRCIALAQLLVEQNFPAAIAHR  
 GMPQEERLSRYQQFKDFQRRILVATNLFGRGMDIERNIAFNNDMPEDSDTYLHRVAR  
 AGRFGTKGLAITFVSDENDAKILNDVQDRFEVNISELPDEIDISSYIEQTR

#### SEQID No:28

MSYAEKPDEITKDEWMEKLNHLHVQRADMNRLIMNYLVTEGFKEAAEKFRMESGIEPS  
 VDLETLDERIKIREMILKGQIQEAIALINSLHPELLDTNRYLYFHLQQQHILIRQRETEAA  
 LEFAQTQLAEQGEESRECLTEMERTLALLAFDSPEESPFGLLHTMQRQKWSEVNQA  
 VLDYENRESTPKLAKLLKLLWAQNELDQKKVKYPKMTDLSKGVIEEPK

#### SEQID No:29

MAMQAAKRANIRLPPEVNRILYIRNLPYKITAEEMYDIFGKYGPIRQIRVGNTPETRGATAY  
 VVYEDIFDAKNACDHLSGFNVCNRYLVVLYYNANRAFAQMDTKKKKEEQLKLLKEYGIN  
 TDPPK

#### SEQID No:30

MRSPATGVPLPTPPPLLLLLLLLLLPPPLLGQDQVGPCRSLSRGRGSSGACAPMGWLC  
 PSSASNLWLYTSRCDAGTELTGHLVPHHDGLRVWCPESEAHIPPAPEGCPWSCR  
 LLGIGGHLSPQGKLTLP EEHPCLKAPRLRCQSCKLAQAPGLRAGERSPEESLGRRKR  
 NVNTAPQFQPPSYQATVPENQPAGTPVASLRAIDPDEGEAGRLEYTMDALFDSRSNQF  
 FSLDPVTGAVTTAEELDRETKSTHVFRVTAQDHGMPRRSALATLTILVTDNDHDPVFE

QQEYKESLRENLEVGYEVLTVRATDGDAPPNANILYRLLEGSGGSPSEVFEIDPRSGVI  
 RTRGPVDREEVESYQLTVEASDQGRDPGPRSTTAAVFLSVEDDNDNAPQFSEKRYVV  
 QVREDVTPGAPVLRVTASDRDKGSNAVHYSIMSGNARGQFYLDAQTGALDVVSPLDY  
 ETTKEYTLRVRAQDGGRPPLSNVSGGLVTVQVLDINDNAPIFVSTPFQATVLESVPLGYLV  
 LHVQAIDADAGDNARLEYRLAGVGHDFPFTINNGTGWISVAAELDREEVDFYSFGVEAR  
 DHGTPALTASASVSVTVLDVNDNNPTFTQPEYTVRLNEDAAVGTSVVTVSAVDRDAHS  
 VITYQITSGNTRNRFSITSQSGGGLVSLALPLDYKLERQYVLAVTASDGTRQDTAQIVVN  
 VTDANTHRPVFQSSHYTVNVNEDRPAGTTVVLISATDEDTGENARITYFMEDSIPQFRID  
 ADTGAVTTQAELDYEDQVSYTLAITARDNGIPQKSDTTYLEILVNDVNDNAPQFLRDSYQ  
 GSVYEDVPPFTSVLQISATDRDSGLNGRVFYTFQGGDDGDGDFIVESTSGIVRTLRLRD  
 RENVAQYVLRAYAVDKGMPPARTPMEVTVTVLDVNDNPPVFEQDEFDVFVEENSPIGL  
 AVARVTATDPDEGTNAQIMYQIVEGNIPEVFQLDIFSGELTALVDLDYEDRPEYVLVIQAT  
 SAPLVSRATVHVRLDRNDNPPVLGNFEILFNHYVTNRSSSFPGGAIGRVP AHDPDISD  
 SLTYSFERGNELSLVLLNASTGELKLSRALDNNRPLEAIMSVLVSDGVH SVTAQCALRVT  
 IITDEMLTHSITLRLEDMSPERFLSPLLGLFIQAVAATLATPPDHVVVFVNVQRD TDAPGGH  
 ILNVSLSVGQPPGPGGGPPFLPSEDLQERLYLNRSLT AISAQRVLPFDDNICLREPCEN  
 YMRCVSVLRFDSSAPFIASSSVLFRPIHPVGGLRCRCPPGFTGDYCETEVDLCYSRPCG  
 PHGRCRSREGGYTCLCRDGYTGEHCEVSARSGRCTPGVCKNGGTCVNLLVGGFKCD  
 CPSGDFEKPYPYCQVTTRSFP AHSFITFRGLRQRHFHTLALS FATKERDGLLLYNGRFNEK  
 HDFVALEVIQEQVQLTFSAGESTTTVSPFVPGGVSDGQWHTVQLKYYNKPLL GQTGLP  
 QGPSEQKVAVVTVDGCDTGVALRFGSVLGNYSCAAQGTQGGSKKSLD LTGPLLLGGV  
 PDLPESEFPVRMRQFVGCMRN LQVDSRHIDMADFIANNGTVPGCPAKKNVCDSNTCHN  
 GGTCVNQWDAFSCECPLGFGGKSCAQEMANPQHFLGSSSLVAWHGLSLPISQPWYLSL  
 MFRTRQADGVLLQAITRGRSTITLQLREGHVMLSVEGTGLQASSLRLEPGRANDGDWH  
 HAQLALGASGGPGHAILSFDY GQQR AEGNLGPRLHGLHLSNITVGGIPGPAGGVARGF  
 RGCLQGVRVSDTPEGVNSLDPSHGESINVEQGCSLPDPCDSNPCPANSYCSNDWDSY  
 SCSCDPGYYGDNCTNVCDLNPCEHQSVCTRKPSAPHGYTCECPPNYLGPYCETRIDQ  
 PCPRGWWGHPTCGPCNCDVSKGFDPCDNKTSGECHCKENHYRPPGSPTCLLCDYCYP  
 TGSLSRVCDPEDGQCPCPKPGVIGRQCDCRCDNPFAEVT TNGCEVNYDSCPRAIEAGIW  
 WPRTRFGLPAAAPCPKGSFGTAVRHCD EHRGWLPPNLFNCTSITFSELKGFAERLQRN  
 ESGLD SGRSQQ LALLLRNATQHTAGYFGSDVKVAYQLATRLLAHESTQRGFGLSATQD  
 VHFTENLLRVGSALLDTANKRHWELIQQTEGGTAWLLQH YEAYASALAQNMRHTYLSP  
 FTIVTPNIVISVVR LDKGNFAGAKLP RYEALRGEQPPDLETTVILPESVFRET PPVVRPAG  
 PGEAQEPEELARRQRRHPELS QGEAVASVIIYRTL AGLLPHNYDPDKRSLRVPKRPIINT

PVVSISVHDDEELLPRALDKPVTVQFRLLTEERTKPICVFWNHHSILVSGTGGWSARGC  
 EVVFRNESHVSCQCQCNHMTSFAVLMDVSRRENGEILPLKTLTYVALGVTLAALLTFFFLT  
 LLRILRSNQHGIRRNLTAAALGLAQLVFLGINQADLPFACTVIAILLHFLYLCTFSWALLEAL  
 HLYRALTEVRDVNTGPMRFYYMLGWGVPAFITGLAVGLDPEGYGNPDFCWLSIYDTLI  
 WSFAGPVAFVAVSMSVFLYILAAASCAAQRQGFEEKGPVSGLQPSFAVLLLLSATWLLA  
 LLSVNSDTLLFHLYLFATCNCIQGPFIFLSYVVLKSKEVRKALKLACSRKPSPDPALTTKSTL  
 TSSYNCPSPYADGRLYQPYGDSAGSLHSTSRSGKSQPSYIPFLLREESALNPGQGPPG  
 LGDPGSLFLEGQDQQHDPDTDSDSLSEDDQSGSYASTHSSDSEEEEEEEEEEEAAAF  
 PGEQGWDSLLGPGAERLPLHSTPKDGGPGPGKAPWPGDFGTTAKESSGNGAPEERL  
 RENGDALESREGSLGPLPGSSAQPHKGILKKKCLPTISEKSSLLRPLEQCTGSSRGSSA  
 SEGSRGGPPPRPPPRQSLQEQLNGVMPIAMSIKAGTVDEDSSGSEFLFFNFLH

SEQID No:31

MLRRPAPALAPAARLLLGLLGGGVWAARVKNHKPWLEPTYHGIVTENDNTVLLDPP  
 LIALDKDAPLRFAESFEVTVTKEGEICGFKIHGQNVPFDAVVVDKSTGEGVIRSKEKLDC  
 ELQKDYSFTIQAYDCGKGPDGTNVKKSHKATVHIQVNDVNEYAPVFKEKSYKATVIEGK  
 QYDSILRVEAVDADCSPQFSQICSYEIITPDVPFTVDKDGYIKNTEKLNYGKEHQYKLTVT  
 AYDCGKKRATEDVLVKISIKPTCTPGWQGWNNRIEYEPGTGALAVFPNIHLETCDPEVA  
 SVQATVELETSBIGKGCDRDTYSEKSLHRLCGAAAGTAELLPSPSGSLNWTMGLPTDN  
 GHDSQVFEFNGTQAVRIPDGVVSVSPKEPFTISVWMRHGPFGRKKETILCSSDKTDM  
 NRHHYSLYVHGCRLIFLRQDPSEEKKYRPAEFHWKLNQVCDEEWHHYVLNVEFPSVT  
 LYVDGTSHEPFSVTEDYPLHPSKIETQLVVGACWQEFSGVENDNETEPVTVASAGGDL  
 HMTQFFRGNLAGLTLRSGKLADKKVIDCLYTCKEGLDLQVLEDSGRGVQIQAHPSQLVL  
 TLEGEDLGELDKAMQHISYLSNRQFPTPGIRRLKITSTIKCFNEATCISVPPVDGYVMVLQ  
 PEEPKISLSGVHHFARAASEFESSEGVFLFPELRIISTITREVEPEGDGAEDPTVQESLVS  
 EEIVHDLDTCEVTVEGEELNHEQESLEVDMARLQQKGIEVSSSELGMTFTGVDTMASY  
 EEVLHLLRYRNWHARSLDRKFKLICSELNGRYISNEFKVEVNVHTANPMEHANHMAA  
 QPQFVHPEHRSFVDLSGHNLANPHPFVVPSTATVVIVCVSFLVFMILGVFRIRAAHR  
 RTMRDQDTGKENEMDWDDSAITITVNPMEYEDQHSSEEEEEEEEEEESEDGEEEDD  
 ITSAESESSEEEEEGEQGDQPQATRQQQLEWDDSTLSY

SEQID No:32

MLPGRLCWVPLLLALGVGSGSGGGGDSRQRRLLAAKVNKHKWPWIETSYHGVITENNDT  
 VILDPPLVALDKDAPVPFAGEICAFKIHGQELPFEAVVLNKTSGEGRLRAKSPIDCELOKE

YTFIIQAYDCGAGPHETA WKKSHKAVVHIQVKDVNEFAPTFKEPAYKAVVTEGKIYDSIL  
 QVEAIDEDCSPQYSQICNYEIVTTDVPFAIDRNGNIRNTEKLSYDKQHQQYEILVTAYDCG  
 QKPAAQDTLVQVDVKPVCKPGWQDWTKRIEYQPGSGSMPLFPSIHLETCDGAVSSLQI  
 VTELQTNYIGKGC DRETYSEKSLQKLCGASSGIIDLLPSPSAATNWTAGLLVDSSEMIFK  
 FDGRQGAKIPDGIVPKNLTDQFTITMWMKHGPPSPGVRAEKETILCNSDKTEMNRHHYAL  
 YVHNCRLVFLLRKDFDQADTFRPAEFHWKLDQICDKEWHYYVINVEFPVVTLYMDGAT  
 YEPYLV TNDWPIHP SHIAMQLTVGACWQGGGEVTKPQFAQFFHGSLASLTIRPGKMESQ  
 KVISCLQACKEGLDINSLES LGQGKIYHFNPSQSILVMEGDDIGNINRALQKVSYINSRQF  
 PTAGVRRLKVSSKVQCFGEDVCISIPEV DAYVMVLQAIEPRITLRGTDHFWRPAAQFES  
 ARGVTLFPDIKIVSTFAKTEAPGDVKTTPKSEVLEEMLHNLD FCDILVIGGDLDP RQECL  
 ELNHSELHQRHLDATNSTAGYSIYGVGSM SRYEQVLH HIRYRNWRPASLEARRFRIKC  
 SELNGRYTSNEFNLEVSILHEDQVSDKEHVNHLIVQPPFLQSVHHPESRSSIQHSSVVP  
 SIATVVIISVCM LVFV VAMGVYRVRIAHQHFIQETEA AKESEMDWDD SALTITVNPMEKH  
 EGP GHGEDETEG EEEEEEA EEEEMSSSSSGSDDSEEEEEEEGMGRGRHGQNGARQAQL  
 EWDDSTLPY

SEQID No:33

MTLLLLPLLLASLLASCSCNKANKHKPWIEAEYQGIVMENDNTVLLNPPLFALDKDAPLR  
 YAGEICGFRLHGS GVPFEAVILDKATGEGLIRAKEPVDCEAQKEHTFTIQAYDCGEGPD  
 GANTKKSHKATVHVRVNDVNEFAPVFVERLYRAAVTEGKLYDRILRVEAIDGDCSPQYS  
 QICYYEILTPNTPFLIDNDGNIENTEKLQYSGERLYKFTVTAYDCGKKRAADDAEVEIQVK  
 PTCKPSWQGW NKRIEYAPGAGSLALFP GIRLETCDEPLWNIQATIELQTSHVAKGCDRD  
 NYSERALRKLCGAATGEVDLLPMPGP NANWTAGLSVHYSQDSSLIYWFNGTQAVQVP  
 LGGPSGLGSGPQDSLS DHFTLSFWMKHGVTPNKGKKEEETIVCNTVQNE DGF SHYSLT  
 VHGCRIAFLYWPLLESARPVKFLWKLEQVC DDEWHHYALNLEFPTVTLYTDGISFDPALI  
 HDNGLIHPPRRPALMIGACWTE EKNKEKEKGDNSTDTTQGDPLSIHHYFHGYLAGFS  
 VRSGRLESREVIECLYACREGLDYRDFESLGKGMKVHVNPSSQLLTLEGDDVETFNHA  
 LQHVAYMNTLRFATPGVRPLRLTTAVKCFSEESCVSIPEVEGYVVVLQPDAPQILLSGTA  
 HFARPAVD FEGTNGVPLFPDLQITCSISHQVEAKKDES WQGTVTDTRMSDEIVHNLDG  
 CEISLVGDDLDPERESLLLDTTSLQQRGLELTNTSAYLTIAGVESITVYEEILRQARYRLR  
 HGAALYTRKFRLSCSEMNGRYSSNEFIVEVNV LHSMNRVAHPSHVLSSQQFLHRGHQP  
 PPEMAGHSLASSHRNSMIPSAATLIIVVCV GFLVLMVVLGLVRIHSLHRRVSGAGGPPGA  
 SSDPKDPDLFWDD SALTII VNPME SYQNRQSCVTGAVGGQQEDEDSSDSEVADSPSS  
 DERRIETPPHRY

SEQID No:34

MYIKQVIIQGFRSYRDQTIVDPFSSKHNIVGRNGSGKSNFFYAIQFVLSDEFSHLRPEQ  
 RLALLHEGTGPRVISAFVEIIFDNSDNRLPIDKEEVSLRRVIGAKKDQYFLDKKMVTKNDV  
 MNLLESAGFSRNPYYIVKQGKINQMATAQDSQRLKLLREVAGTRVYDERKEESISLMK  
 ETEGKREKINELLKYIEERLHTLEEEKEELAQYQKWDKMRRALEYTIYNQELNETRAKLD  
 ELSAKRETSGEKSQRQLRDAQQDARDKMEDIERQVRELKTKISAMKEEKEQLSAERQEQ  
 IKQRTKLELKAKDLQDELGNSEQRKRLKERQKLEKIEEKQKELAETEPKFNSVKEKE  
 ERGIARLAQATQERTDLYAKQGRGSQFTSKEERDKWIKKELKSLDQAINDKKRQIAAIHK  
 DLEDTEANKEKNLEQYNKLDQDLNEVKARVEELDRKYEEVKNKKDELQSERNYLWREE  
 NAEQQALAAKREDLEKKQQLLRAATGKAILNGIDSINKVLDHFRRKGINQHVQNGYHGIV  
 MNNFECEPAFYTCVEVTAGNRLFYHIVDSDEVSTKILMEFNKMNLPGVETFLPLNKLDV  
 RDTAYPETNDAIPMISKLRYNPRFDKAFKHVFGKTLICRSMEVSTQLARAFTMDCITLEG  
 DQVSHRGALTGGYYDTRKSRLELQKDVRKAEEELGELEAKLNENLRNRIERINNEIDQL  
 MNQMQQIETQQRKFKASRDSILSEMMLKEKRQQSEKTFMPKQRSLSLEASLHAME  
 STRESLKAELGTDLLSQLSLEDQKRVDALNDEIRQLQQENRQLLNERIKLEGIITRVETYL  
 NENLRKRLDQVEQELNELRETEGGTVLTATTSELEAINKRVKDTMARSEDLDNSIDKTE  
 AGIKELQKSMERWKNMEKEHMDAINHDTKELEKMTNRQGMLLKKKEECMKKIRELGSL  
 PQEAFEKYQTLSLKQLFRKLEQCNTTELKKYSHVNKKALDQFVNFSEQKEKLIKREQEELD  
 RGYKSIMELMNVLELRKYEAIQLTFKQVSKNFSEVFQKLVPGGKATLVMKKGDVEGSQS  
 QDEGEGSGESERGSQSQSSVPSVDQFTGVGIRVSFTGKQGEMREMQQLSGGQKSLV  
 ALALIFAIQKCDPAPFYLFDEIDQALDAQHRKAVSDMIMELAVHAQFITTTFRPELLESAD  
 KFYGVKFRNKVSHIDVITAEMAKDFVEDDTTHG

SEQID No:35

MAVTLDDKDAYYRRVKRLYSNWRKGEDEYANVDAIVVSVGVDEEIVYAKSTALQTWLFG  
 YELTDTIMVFCDDKIIFMASKKKKVEFLKQIANTKGNENANGAPAITLLIREKNESNKSSFD  
 KMIEAIKESKNGKKIGVFSKDKFPGFEMKSWNDCLNKEGFDKIDISAVVAYTIAVKEDGE  
 LNLMKKAASITSEVFNFKFFKERVMEIVDADEKVRHSLAESVEKAIEEKKYLAGADPSTV  
 EMCYPPIIQSGGNYNLKFSSVSDKNHMHFGAITCAMGIRFKSYCSNLVRTLMVDPSQEV  
 QENYNFLLQLQEELLKELRHGVKICDVYNAVMDVVKKQKPELLNKITKNLGFGMGIEFR  
 EGSLVINSKNQYKLKKGMVFSINLGFSDLTNKEGKKPEEKTYALFIGDTVLVDEDGPATV  
 LTVSKKKVKNVGIFLKNEDEEEEEEEEKDEAEDLLGRGSRAALLTERTRNEMTAEKRRRA  
 HQKELAAQLNEEAKRRLTEQKGEQQIQKARKSNVSYKNPSLMPKEPHIR



EMKIYIDKKYETVIMPVFGIATPFHIATIKNISMVEGDYTYLRINFYCPGSALGRNEGNIF  
 PNPEATFVKEITYRASNIKAPGEQTPALNLQNAFRIIKEVQKRYKTREAEKEKEGIVKQ  
 DSLVINLNRSNPKLDLYIRPNIAQKRMQGSLEAHVNGFRFTSVRGDKVDILYNNIKHAL  
 FQPCDGEMIIVLHFHLKNAIMFGKKRHTDVQFYTEVGEITTDLGKHQHMHDRDDLYAEQ  
 MEREMRHKLKTAFAKNFIEKVEALTKEELEFEVPFRDLGFNGAPYRSTCLLQPTSSALVN  
 ATEWPPFVVTLDLEVELHFERVQFHLKNFDMVIVYKDYSKKVTMINAIPVASLDPIKEWLN  
 SCDLKYTEGVQSLNWTKIMKTIVDDPEGFFEQGGWSFLEPEGEGSDAEEGDSESEIED  
 ETFNPSEDDYEEEEEDSDEDYSSEAEESDYSKESLGSEEEESGKDWDELEEEARKADR  
 ESRYYYYEEQSRSMSRKRKASVHSSGRGSGNRGSRHSSAPPKKKRK

SEQID No:36

MVVSKMNKDAQMRAAINQKLIETGERERLKELLRAKLIECGWKDQLKAHCKEVIKEKGL  
 EHVTVDDLVAEITPKGRALVPDSVKKELLQRIRTFLAQHASL

SEQID No:37

MENHKSNNKENITIVDISRKINQLPEAERNLLENGSVYVGLNAALCGLIANSLFRRILNVT  
 KARIAAGLPMAGIPFLTTLTYRCFVSFPLNTGDLDCETCTITRSGLTGLVIGGLYPVFLAI  
 PVNGGLAARYQSALLPHKGNILSYWIRTSKPVFRKMLFPILLQTMFSAYLGSEQYKLLIK  
 ALQLSEPGKEIH

SEQID No:38

MAEVEETLRLQSQKGVQGIIVNTEGIPIKSTMDNPTTTQYASLMHSFILKARSTVRDID  
 PQNDLTFLRIRSKKNEIMVAPDKDYFLIVIQNPTE

SEQID No:39

MAAVGRVGSFGSSPPGLSSTYTGGPLGNEIASGNNGGAAAGDDEDGQNLWSCILSEVS  
 TRSRSKLPAGKNVLLLGEDGAGKTSLIRKIQQIEEYKKGRGLELYLNVHDEDRDDQTR  
 CNVWILDGDLYHKGLLKFSLDVSLKDTLVMLVVDMSKPWTALDSLQKWASVVREHVD  
 KLKIPPEEMKQMEQKLIRDFQEYVEPGEDFPASPQRRNTASQEDKDDSVVVPLGADTL  
 THNLGIPVLVCTKCDASVLEKEHDYRDEHDFDFQSHIRKFCRLRYGAALIYTSVKENKNI  
 DLVYKYIVQKLYGFPYKIPAVVVEKDAVFIPAGWDNDKKIGILHENFQTLKAEDNFEDIITK  
 PPVRKFVHEKEIMAEDDQVFLMKLQSLAKQPPTAAGRPVDASPRVPGGSPRTPNRSV  
 SSNVASVSPIPAGSKKIDPNMKAGATSEGVLANFFNSLLSKKTGSPGGPGVSGGSPAG  
 GAGGGSSGLPPSTKKSGQKPVLDVHAELDRIKRPVTVSPTTPTSPTEGEAS

## SEQID No:40

MVTQILGAMESQVGGGPAGPALPNGPLLGTNGATDDSKTNLIVNYLPQNMTQDEFKSL  
 FGSIGDIESCKLVRDKITGQSLGYGFVNYS DPNDADK AINTLNGLKLQTKTIKVS YARPSS  
 ASIRDANLYVSGLPKTMSQKEMEQLFSQYGRITSRILVDQVTGVS RGVGFIRFDK RIEA  
 EEAIKGLNGQKPLGAAEPITVKFANNPSQKTGQALLTHLYQSSARRYAGPLHHQTQRFR  
 LDNLLNMAYGVKSPLSLIARFSP I AIDGMSGLAGVGLSGGAAGAGWCIFVYNLSPEADE  
 SVLWQLFGPFGAVTNVKVIRDFTTNKCKGFGFVTMTNYDEAAMAIASLNGYRLGERVL  
 QVSFKTSKQHKA

## SEQID No:41

MVCTCVEGDNQFIVTEIPHVRQLISGDGVGEC A VRAATEGRTLILEGLEKAERNVLPVLN  
 NLENREM QLEDGRFLMSAERYDKLLRDHTKKELDSWKIVRVSENFRVIALGLPVPRYS  
 GNPLDPPLRSRFQARDIYYLPFKDQLKLLYSIGANVSAEKVSQLLSFATTLCSQESSTLG  
 LPDFPLDSLAAAVQILDSFPMMPIKHAIQWLYPYSILLGHEGKMAVEGV LKRFELQDSGS  
 SLLPKEIVKVEKMMENHVSQASVTIRIADKEVTIK

## SEQID No:42

MSASQDSRSRDNGPDGMEPEGVIESNWN EIVDSFDDMNLSESLLRGIYAYGF EKPSAI  
 QQRAILPCIKGYDVIAQAQSGTGKTATFAISILQQIELDLKATQALVLAPTRELAQQIQKV  
 MALGDYMGASCHACIGGTNVRAEVQKLQMEAPHIIVGTPGRVFDMLNRRYLSPKYIKM  
 FVLDEADEMLSRGFKDQIYDIFQKLNSNTQVVLLSATMPSDVLEVTKKFMRDP I RILVKK  
 EELTLEGIRQFYINVEREEWKLDTLCDLYETLTITQAVIFINTRRKVDWLTEKM HARDFTV  
 SAMHGDMDQKERDVIMREFRSGSSRVLITTDLLARGIDVQQVSLVINYLPTNRENYIH  
 RIGRGGRFGRKGVAINMVTEEDKRTL RDIETFYNTSIEEMPLNVADLI

## SEQID No:43

MDQCVTVERELEKVLHKFSGYGQLCERGLEELIDYTGGLKHEILQSHGQDAELSGTSL  
 VLTQCCKRIKDTVQKLASDHKDIHSSVSRVGKAIDKNFDS DISSVGIDGCWQADSQRLL  
 NEVMVEHFFRQGM LDVAEELCQESGLSVDP SQKEPFVELNRILEALKVRVLRPALEWA  
 VSNREMLIAQNSSLEFKLHRLYFISLLMG GTTNQREALQYAKNFQPFALNHQKDIQVLM  
 GSLVYLRQGIENSPYVHLLDANQWADICDIFTRDACALLGLSVESPLSVSFSAGCVALPA  
 LINIKAVIEQRQCTGVWNQKDELPIEVDLGKKCWYHSIFACPI LRQQT DNNPPMKLVCG  
 HIISRDALNKM FN GSKLKCPYCPMEQSPGDAKQIFF

SEQID No:44

MLGTGPAAATTAATTSSNVSVLQQFASGLKSRNEETRAKAAKELQHYYVTMELREMSQE  
 ESTRFYDQLNHHIFELVSSSDANERKGGILAIASLIGVEGGNATRIGRFANYLRNLLPSND  
 PVVMEMASKAIGRLAMAGDTFTA EYVEFEVKRALEWLGADRNEGRRHAAVLVLRELAI  
 SVPTFFFQQVQPFFDNIFVAVWDPKQAIREGAVAALRACLITTTQREPKEMQKPQWYR  
 HTFEEAEKGFDETLAKEKGMNRDDRIHGALLILNELVRISSMEGERLREEMEEITQQQLV  
 HDKYCKDLMGFGTKPRHITPFTSFQAVQPQQSNALVGLLGYSSHQGLMGFGTSPSPAK  
 STLVESRCCRDLMEEKFDQVCQWVLKCRNSKNSLIQMTILNLLPRLAAFRPSAFTDTQY  
 LQDTMNHVLSVCVKKEKERTA AFQALGLLSVAVRSEFKVYLPRVLDIIRAALPPKDFAHKR  
 QKAMQVDATVFTCISMLARAMGPGIQQDIKELLEPMLAVGLSPALTAVLYDLSRQIPQLK  
 KDIQDGLLKMLSLVLMHKPLRHPGMPKGLAHQLASPGLTTLPEASDVGSITLALRTLGSF  
 EFEGHSLTQFVRHCADHFLNSEHKEIRMEAARTCSRLTPSIHLISGHAHVVSQTAVQV  
 VADVLSKLLVVGITDPDPDIRYCVLASLDERFDAHLAQAEENLQALFVALNDQVFEIRELAI  
 CTVGRLSSMNP AFVMPFLRKMLIQILTELEHSGIGRIKEQSARMLGHLVSNAPRLIRPYM  
 EPILKALILKLKDPDPDPNPGVINNVLATIGELAQVSGLEMRKWVDELFIIMDMLQDSSLL  
 AKRQVALWTLGQLVASTGYVVEPYRKYPTLLEVLLNFLKTEQNQGTTRREAIRVLGLLGA  
 LDPYKHKVNIGMIDQSRDASAVSLSESKSSQDSSDYSTSEMLVNMGNLPLDEFYPAVS  
 MVALMRIFRDQSLSHHHTMVVQAITFIFKSLGLKCVQFLPQVMPTFLNVIRVCDGAIREF  
 LFQQLGMLVSFVKSHIRPYMDEIVTLMREFWVMNTSIQSTIILLIEQIVVALGGEFKLYLPQ  
 LIPHMLRVFMHDNSPGRIVSIKLLAAIQLFGANLDDYLHLLLPPIVKLFDAP EAPLPSRKAA  
 LETVDRLTESLDFTDYASRIIHPIVRTL DQSPELRSTAMDTLSSLVFQLGKKYQIFIPMVNK  
 VLVRHRINHQR YDVLICRIVKGYTLADEEEDPLIYQHRMLRSGQG DALASGPVETGPMK  
 KLHVSTINLQKAWGAARRVSKDDWLEWLRRLSLELLKDSSSPSLRSCWALAQAYNPMA  
 RDLFNAAFVSCWSELNEDQQDELIRSIELALTSQDIAEVTQTLLNLAEFMEHSDKGPLPL  
 RDDNGIVLLGERAAKCRAYAKALHYKELEFQKGPTPAILES LISINNKLQQPEAAAGVLE  
 YAMKHFGELEIQATWYEKLHEWEDALVAYDKKMDTNKDDPELMLGRMRCLEALGEWG  
 QLHQQCCEKWTLVNDETQAKMARMAAAAAWGLGQWDSMEEYTCMIPRDTHDGAFY  
 RAVLALHQDLFSLAQQCIDKARDLLDAELTAMAGESYSRAYGAMVSCHMLSELEEVIQY  
 KLVPERREIIRQIWWERLQGCQRIVEDWQKILMVRSLVSPHEDMRTWLKYASLCGKS  
 GRLALAHKTLVLLLGVDP SRQLDHPLPTVHPQV TYAYMKNMWKSARKIDAFQHMQH FV  
 QTMQQQAQHAIATEDQQHKQELHKLMARCFKLGEWQLNLQGINESTIPKVLQYYSA  
 TEHDRSWYKAWHAWAVMNFEAVLHYKHQNQARDEKKLRHASGANITNATTAATTAA  
 TATTTASTE GSNSESEAESTENSPTPSPLQKKVTEDLSKTLLMYTVP AVQGGFFRSISLSR

GNNLQDTRLRVLTWFDYGHWPDVNEALVEGVKAIQIDTWLQVIPQLIARIDTPRPLVGRL  
 IHQLLTDIGRYHPQALIYPLTVASKSTTTARHNAANKILKNMCEHSNTLVQQAMMVSEELI  
 RVAILWHEMWHEGLEEASRLYFGERNVKGMFEVLEPLHAMMERGPQTLKETSFNQAY  
 GRDLMEAEWCRKYMKSGNVKDLTQAWDLYYHVFRISKQLPQLTSLELQYVSPKLL  
 MCRDLELAVPGTYDPNQPIIRIQSIAPSLQVITSKQRPRKLTLMGSNGHEFVFLKGGHED  
 LRQDERVMQLFGLVNTLLANDPTSLRKNLSIQRYAVIPLSTNSGLIGWVPHCDTLHALIR  
 DYREKKKILLNIEHRIMLRMAPDYDHLTLMQKVEVFEHAVNNTAGDDLAKLLWLKSPSS  
 EVWFDRRTNYTRSLAVMSMVGILGLGDRHPSNMLDRLSGKILHIDFGDCFEVAMTR  
 EKFEKIPFRLTRMLTNAMEVTGLDGNRYRITCHTVMEVLREHKDSVMAVLEAFVYDPLL  
 NWRLMDTNTKGNKRSRTRTDSYSAGQSVEILDGVELGEPAHKKTGTTVPESIHFIGD  
 GLVKPEALNKKAIQIINRVRDKLTGRDFSHDDTLDVPTQVELLIKQATSHENLCQCYIGW  
 CFW

SEQID No:45

MMNNSGYSDAGLGLGDETDEMPSTEKDLAEDAPWKKIQQNTFTRWCNEHLKCVGKRL  
 TDLQRDLSDGLRLIALLEVLSQKRMRYKFHPRPNFRQMKLENVSVALEFLEREHIKLVSI  
 DSKAIVDGNLKLILGLIWTILHYSISMPMWEDEDEDARKQTPKQRLLGWIQNKVPQLPI  
 TNFNRDWQDGKALGALVDNCAPGLCPDWEAWDPNQPVENAREAMQQADDWLGVQP  
 VIAPEEIVDPNVDEHSVMTYLSQFPKAKLKPAPVRSKQLNPKKAIAYGPGIEPQGNTVL  
 QPAHFTVQTVDAGVGEVLVYIEDPEGHTEEAKVVPNNDKDRTYAVSYVPKVAGLHKVT  
 VLFAGQNIERSPFVNVGMALGDANKVSARGPGLEPVGNVANKPTYFDIYTAGAGTGD  
 VAVVIVDPQGRRDTVEVALEDKGDSTFRCTYRPAMEGPHTVHVAFAGAPITRSPFPVH  
 VSEACNPNA CRASGRGLQPKGVRVKEVADFKVFTKGAGSGELKVTVKGPKGTEEPVK  
 VREAGDGVFECEYYPVVPGKYVVTITWGGYAI PRSPFEVQVSPEAGVQKVRAWGPGL  
 ETGQVGKSAD FVVEAIGTEVGT LGFSIEGPSQAKIECDDKGDGSCDVRYWPTEPGEYA  
 VHVICDDEDIRDSPFIAHILPAPPDCFPDKVKAFGPGLEPTGCIVDKPAEFTIDARAAGKG  
 DLKLYAQDADGCPIDIKVIPNGDGTFRCSYVPTKPIKHTIIISWGGVNVPKSPFRVNVGEG  
 SHPERVKVYGPVVEKTGLKANEPTYFTVDCSEAGQGDSIGIKCAPGVVGP AEADIDFD  
 IIKNDNDTFTVKYTPPGAGRYTIMVLFANQEIPASPFHIKVDP SHDASKVKAEGPGLNRT  
 GVEVGKPTHFTVLT KGAGKAKLDVQFAGTAKGEVVRDFEIIDNHDYSYTVKYTAVQQG  
 NMAVTVTYGGDPVPKSPFVVNVAPPLDSLKIKVQGLNSKVAVGQEQAFSVNTRGAGG  
 QGQLDVRMTSPSRRPIPCKLEPGGGAEAAVRYMPPEEGPYKVDITYDGHPVPGSPF  
 AVEGVLPPDPSKVCAYGPGLKGGLVGTPAPFSIDTKGAGTGGLGLTVEGPCEAKIECQ  
 DNGDGSCAVSYLPTEPGEYTINILFAEAHIPGSPFKATIRPVFDPSKVRASGPGLERGKV

GEATFTVDCSEAGEAELTIEILSDAGVKAEVLIHNNADGTYHITYSPAFFPGTYTITIKYGG  
 HPVPKFPTRVHVQPAVDTSQGVKVSQPGVEPHGVLREVTTEFTVDARSLTATGGNHVTA  
 RVLNPSGAKTDTYVTDNGDGTYRVQYTAYEEGVHLVEVLYDEVAVPKSPFRVGVTEGC  
 DPTRVRAFGPGLEGGLVNKANRFTVETRAGAGTGGLGLAIEGPSEAKMSCKDNKDGSC  
 TVEYIPFTPGDYDVNITFGGRPIPGSPFRVPVKDVVDPGKVKCSGPGLGAGVRARVPQT  
 FTVDCSQAGRAPLQVAVLGPVGVAEPVEVRDNGDGTHTVHYTPATDGPYTVAVKYAD  
 QEVPRSPFKIKVLPAMDASKVRASGPGLNASGIPASLPVEFTIDARDAGEGLLTVQILED  
 PEGKPKKANIRDNGDGTYTVSYLPDMSGRYTITIKYGGDEIPYSPFRIHALPTGDASKCL  
 VTVSIGGHGLGACLGPRIQIGQETVITVDAKAAGEGKVTCTVSTPDGAELDVDVVENHD  
 GTFDIYYTAPEPGKYVITIRFGGEHIPNSPFHVLACDPLPHEEEPSEVPQLRQPYAPPRP  
 GARPTHWATEEPVVPVEPMESMLRPFNLVIPFAVQKGELTGEVRMPSPGKTARPNITDN  
 KDGTITVRYAPTEKGLHQMGIKYDGNHIPGSPLQFYVDAINSRLHVSAYGPGLSHGMVVK  
 PATFTIVTKDAGEGGLSLAVEGPSKAEITCKDNKDGTCVSYLPATPGDYSIIVRFDDKHI  
 PGSPFTAKITGDDSMRTSQLNVGTSTDVSLKITESDLSQLTASIRAPSGNEEPCLLKRLP  
 NRHIGISFTPKEVGEHVSVVRKSGKHVTNSPFKILVGPSEIGDASKVRVWGKGLSEGHT  
 FQVAEFIVDTRNAGYGGLGLSIEGPSKVDINCEMEDGTCKVTYCPTEPGTYIINIKFADK  
 HVPGPSFTVKVTGEGRMKESITRRRQAPSIATIGSTCDLNLKIPGNWFQMVSAQERLTR  
 TFTRSSHTYTRTERTEISKTRGGETKREVRVEESTQVGGDPFPAVFGDFLGRERLGSF  
 GSITRQQEAGEASSQDMTAQVTSPSGKVEAAEIVEGEDSAYSVRFPQEMGPHTVAVKY  
 RGQHVPGPSPFQFTVGPLGEGGAHKVRAGGTGLERGVAGVPAEFSIW TREAGAGGLSI  
 AVEGPSKAEIAFEDRKDGSCGVSYYVQEPGDYEVSIFNDEHIPDSPFVVPVASLSDDA  
 RRLTVTSLQETGLKVNQPASFAVQLNGARGVIDARVHTPSGAVEECYVSELDSKHTIR  
 FIPHENGVSIDVKFNGAHIPGPSPFKIRVGEQSQAGDPGLVSAYGPGLEGGTTGVSSEFI  
 VNTLNAGSGALSVTIDGPSKVQLDCRECEGHVVITYTPMAPGNYLIAIKYGGPQHIVGS  
 PFKAKVTGPRLSGGHSLHETSTVLVETVTKSSSSRGSSYSSIPKFSSDASKVVTRGPGL  
 SQAFVGQKNSFTVDCSKAGTNMMMVGVHGPKTPCEEVYVKHMGNRVYNVTYTVKEK  
 GDYILIVKWGDESVPGPSPFKVKVP

SEQID No:46

RQAWHEVAAPSWRGARLVQSALRVWQVGPHVARERVIPFSSLLGFQRRRCVSCVAGS  
 AFSGPRLASASRSNGQGSALDHFLGFSQPDSSVTPCVPVAVSMNRDEQDVLLVHHPDM  
 PENSRLRVVLLGAPNAGKSTLSNQLLGRKVFPVSRKVHTTRCQALGVITEKETQVILLD  
 TPGIISPGKQKRHHLELSLLEDPWKSMESADLVVVLVDVSDKWTRNQLSPQLLRCLTKY  
 SQIPSVLVMNKVDCLKQKSVLLELTAALTEGVVNGKKLKMQRQAFHSHPGTHCPSPAVK

DPNTQSVGNPQRIGWPHFKEIFMLSALSQEDVKTLKQYLLTQAQPGPWEYHSAVLTSQ  
TPEEICANIIREKLLLEHLPQEVYPNVQOKTAVWEEGPGGELVIQQKLLVPKESYVKLLIGP  
KGHVISQIAQEAGHDLMDIFLCDVDIRLSVKLLK

SEQID No:47

MAAACRSVKGLVAVITGGASGLGLATAERLVGQGASAVLLDLPNSGGGEAQAKKLGNNC  
VFAPADVTSEKDVQQTALALAKGKFGFRVDVAVNCAGIAVASKTYNLKKGQHTLTLEDFQRV  
LDVNLMGTFNVIRLVAGEMGQNEPDQGGQRGVIINTASVAAFEGQVQQAAYSASKGGI  
VGMTLPIARDLAPIGIRVMTIAPGLFGTPLLTSLPEKVCNFLASQVPFPSRLGDPAEY AHL  
VQAIENPFLNGEVIRLDGAIRMQP

SEQID No:48

MAYSQGGGKKKVCYYYDGDIGNYYYGQGHMCKPHRIRMTHNLLLNYGLYRKMEIYRP  
HKATAEEMTKYHSDEYIKFLRSIRPDNMSEYSKQMHIFNVGEDCPAFDGLFEFCQLSTG  
GSVAGAVKLNRRQQTDMAVNWAGGLHHAKKYEASGFCYVNDIVLAILELLKYHQRVLYID  
IDIHHGDGVVEAFYTTDRVMTVSFHKYGEYFPGTGDLRDIGAGKGKYYAVNFPMCDGID  
DESYGQIFKPIISKVMEMYQPSAVVLQCGADSLSGDRLGCFNLTVKGHAKCVEVVKTFN  
LPLLMLGGGGYTIRNVARCWYETAVALDCEIPNELPYNDYFEYFGPDFKLHISPSNMT  
NQNTPEYMEKIKQRLFENLRMLPHAPGVQMQAIPEDAVHEDSGDEDEDGEDPDKRISIRA  
SDKRIACDEEFSDSEDEGEGERNRVADHKKGAKKARIEEDKKETEDKKTDVKEEDKSK  
DNSGEKTDTKGTKSEQLSNP

SEQID No:49

MPSESFCLAAQARLDSKWLKTDIQLAFTRDGLCGLWNEMVKDGEIVYTGTESTQNGEL  
PPRKDDSVESGTTKKEDLNDKEKKDEEETPAPIYRAKSILDSWVWGKQPDVNELKECL  
SVLVKEQQALAVQSATTTLSALRLKQRLVILERYFIALNRTVFQENVKVKWKSSGISLPP  
VDKKSSRPAGKGVEGLARVGSRAALSFAFAFLRRAWRSGEDADLCSELLQESLDALRA  
LPEASLFDESTVSSVWLEVVERATRFLRSVVTGDVHGTPATKGPGSIPLQDQHLALAILL  
ELAVQRGTLSQMLSAILLLLQLWDSGAQETDNERSAQGTSAPLLPLLQRFQSIICRKDAP  
HSEGDMHLLSGPLSPNESFLRYLTLPQDNELAILDRQTAVVMAHLDRLATPCMPPLCS  
SPTSHKGSQEVIGWGLIGWKYYANVIGPIQCEGLANLGVTVIACAERFLILSRNGRVY  
TQAYNSDTLAPQLVQGLASRNIVKIAAHSDDGHYLLAATGEVYSWGCGDGGRLGHGD  
TVPLEEPKVISAFSGKQAGKHVVHIACGSTYSAITAEGELYTWGRGNYGRLGHGSSSED  
EAIPMLVAGLKGLKVIDVACGSGDAQTLAVTENGQVWSWGDGDYGKLGRGGSDGCKT

PKLIEKLQDLVDVVKVRCGSQFSIALTKDGQVYSWGKGDNQRLGHGTEEHVRYPKLLEG  
 LQGKKVIDVAAGSTHCLALTEDSEVHSWGSNDQCQHFDTLRVTKPEPAALPGLDTKHIV  
 GIACGPAQSFAWSSCSEWSIGLRVPFVVDICSMTFEQLDLLLLRQVSEGMDGSADWPPP  
 QEKECVAVATLNLLRLQLHAAISHQVDPEFLGLGLGSILLNSLKQTVVTLASSAGVLSTV  
 QSAAQAVLQSGWSVLLPTAEERARALSALLPCAVSGNEVNISPGRRFMIDLLVGSLMAD  
 GGLESALHAAITAEIQDIEAKKEAQKEKEIDEQEANASTFHRSRTPLDKDLINTGICESSG  
 KQCLPLVQLIQQLLRNIASQTVARLKDVARRISSCLDFEQHSRERSASLDWLLRFQRLLI  
 SKLYPGESIGQTSDISSPELMGVGSLLKKYTALLCTHIGDILPVAASIASTSWRHFAEVAYI  
 VEGDFTGVLLPELVVSIVLLLSKNADLMQEAGAVPLLGGELLEHLDRFNHLAPGKERDDH  
 EELAWPGIMESFFTGQNCRNNEEVTLIRKADLENHNKDGGFWTVIDGKVYDIKDFQTQS  
 LTGNSILAQFAGEDPVVALEAALQFEDTRESMHAFQVGGQYLEPDQEIVTIPDLGSLSSPLI  
 DTERNLGLLLGLHASYLAMSTPLSPVEIECAKWLOSSIFSGGLQTSQIHRYRYNEEKDED  
 HCSSPGGTPASKSRLCSHRRALGDHSQAFLQAIADNNIQDHNVKDFLCQIERYCRQCH  
 LTPIMFPPEHPVEEVGRLLLCCLLKHEDLGHVALSLVHAGALGIEQVKHRTLPKSVVDV  
 CRVYQAKCSLIKTHQEQGRSYKEVCAPVIERLRFLFNELRPAVCNDLSIMSKFKLLSSL  
 PRWRRIAQKIIRERRKKRVPKPKPESMDDEEKIGNEESDLEEACILPHSPINVDKRPIAICS  
 PKDKWQPLLSTVTGVHKKYKWLKQNVQGLYPQSPLLSTIAEFALKEEPVDVEKMRKCLL  
 KQLERAQVRLEGIDTILKLASKNFLLPSVQYAMFCGWQRLIPEGIDIGEPLTDCLKDVDLI  
 PPFNRMLLEVTFGKLYAWAVQNIIRNVLMIDASATFKELGIQPVPLQTITNENPSGPSLGTI  
 PQARFLLVMLSMLTLQHGANNDLLLNSGMLALTQTALRLIGPSCDNVEEDMNASAQG  
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 GELGEDGWIRVQWDTGSTNSYRMGKEGKYDLKLAELPAAAQPSAEDSDTEDDSEAEQ  
 TERNIHPTAMMFTSTINLLQTLCLSAGVHAEIMQSEATKTLGGLLRMLVESGTTDKTSSP  
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 LAVHLLQAVLPWDKTERARDMKCLVEKLFDLGLSLLTTCSSDVPLLRESTRRRRRVRP  
 QASLTATHSSTLAEVVALRLTLHSLTQWNGLINKYINSQLRSITHSFVGRPSEGAQLED  
 YFPDSENPEVGGLMAVLAVIGGIDGRLRLGGQVMHDEFEGEGTVTRITPKGKITVQFSDM  
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 SGNASSLPGEALVGWLLDHSDIQVTELSADTVSDEYSDEEVVEDVDDAAYSMSSTGA  
 VVTESQTYKKRADFLSNDDYAVYVRENIQVGMMVRCCRAYEEVCEGDVGKVIKLD RDG  
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SVTHQSVGVVKAFSANGKDIIVDFPQQSHWTGLLSEMELVPSIHPGVTCDCGCMFPING  
SRFKCRNCDDDFCETCFKTKKHNRHTFGRINEPGQSAVFCGRSGKQLKRCHSSQP  
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DDGKLGHFSRMNCDKPRLIEALKTKRIRDIACGSSHSAALTSSGELYTWGLGEYGR LGH  
GDNTTQLKPKMKVLLGHRVIQVACGSRDAQTLALTDEGLVFSWGDGDFGKLGRGGS  
EGCNIPQNIERLNGQGVQCIECGAQFSLALTKSGVWWTWGKGDYFRLGHGSDVHVRK  
PQVVEGLRGKKIVHVAVGALHCLAVTDSGQVYAWGDNDHGQQGNGTTTVNRKPTLVQ  
GLEGQKITRVACGSSHSVAWTTVDVATPSVHEPVLFQTARDPLGASYLGVPDADSSA  
ASNKISGASNSKPNRPSLAKILLSLDGNLAKQQALSHILTALQIMYARDAVV GALMPAAMI  
APVECP SFSSAAPSDASAMASPMNGEECMLAVDIEDRLSPNPWQEKREIVSSEDAVTP  
SAVTPSAPSASARPFIPVTDDLGAASIIAETMTKTKEDVESQNKAAGPEPQALDEFTSLI  
ADDTRVVVDLLKLSVCSRAGDRGRDVL SAVLSGMGTAYPQVADM LLELCVTELEDVAT  
DSQSGRLSSQPVVVESSHYPYTDSTSGTVKIPGAEGLRVEFDRQCSTERRHDPLTVM  
DGVNRIVSVRSGREWSDWSSEL RIPGDELKWKFISDGSVNGWGWRFTVYPIMPAAGP  
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LPRLFLDEVAKKIRELMADSENMDVLHESHDIKREQDEQLVQWMNRRPDDWTLSAG  
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TGYGAGGRLGIGGTESVSTPTLLESIQHVFIIKKVAVNSGGKHCLALSSEGEVYSWGEAE  
DGKLGHGNRSPCDRPRVIESLRGIEVVDVAAGGAHSACVTAAGDLYTWGKGRYGR LG  
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RRPRQVQGLQGKKVIAIATGSLHCVCCTEDGEVYTWGDNDEGQLGDGTTNAIQRPRLV  
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HLSELFPCIPMFDLEGS LDETGLGPSVGFDTLRGILISQGKEAAFRKV VQATMVRDRQ  
HGPVVELNRIQVKRSRSKGLAGPDGTKSVFGQMCAKMSSFGPDSL LPHRVWKVKF  
VGESVDDCGGGYSESIAEICEELQNGLTPLLIVTPNGRDESGANRDCYLLSPAARAPVH  
SSMFRFLGVLLGIAIRTGSP LSLNLAEPVWKQLAGMSLT IADLSEVDKDFIPGLMYIRDNE  
ATSEEF EAMSLPFTVPSASGQDIQLSSKHTHITLDNRAEYVRLAINYRLHEFDEQVA AVR



EGMARVVPVPLLSLFTGYELETMVCGSPDIPLHLLKSVATYKGIEPSASLIQWFWWEVME  
SFSNTERSLFLRFVWGRTRLPRTIADFRGRDFVIQVLDKYNPPDHFLPESYTCFFLLKLP  
RYSCKQVLEEKLYAIHFCKSIDTDDYARIALTGEPAAADDSSDDSDNEDVDSFASDSTQ  
DYLTGH

SEQID No:50

MICTFLRAVQYTEKLHRSSAKRLLLPIYVLNKACLKTEPSLRGLQYQKKTLRPRCILGVT  
QKTIWTQGPSRKAKEDGSKQVSVHRSQRGGTAVPTSQKVKEAGRDFTYLIVVLFGISI  
TGGLFYTIFKELFSSSSPSKIYGRALEKCRSHPEVIGVFGESVKGYGEVTRRGRRRQHVR  
FTEYVKDGLKHTCVKFYIEGSEPGKQGTVYAQVKENPGSGEYDFRYIFVEIESYPRRTIII  
EDNRSQDD

SEQID No:51

MAATSGTDEPVSGELVSVAHALSIPAESYGNDPDIEMAWAMRAMQHAEVYYKLISVD  
PQFLKLT KVDDQIYSEFRKNFETLRIDVLDPEELKSESAKEKWRPFCLKFNGIVEDFNYG  
TLLRLDCSQGYTEENTIFAPRIQFFAIEIARNREGYNKAVYISVQDKEGEKGVNNGGEKR  
ADSGEEENTKNGGEKGADSGEEKEEGINREDKTDKGGEKGKEADKEINKSGEKAM

SEQID No:52

MSQRDTLVHLFAGGCGGTVGAILTCPLEVVKTRLQSSSVTLYISEVQLNTMAGASVNRV  
VSPGPLHCLKVILEKEGPRSLFRGLGPNLVGVAPSRAIYFAAYSNCKEKLNDVFDPDST  
QVHMISAAMAGFTAITATNPWLKTRLQLDARNRGERRMGAFECVRKVYQTDGLKGFY  
RGMSASYAGISETVIHFVIYESIKQKLLEYKTASTMENGEESVKEASDFVGMMLAAATSK  
TCATTIAYPHVVRTRLREEGTKYRSFFQTL SLLVQEEGYGSLYRGLTTHLVRQIPNTAIM  
MATYELVVYLLNG

SEQID No:53

MSQFKRQRINPLPGGRNFSGTASTSLLGPPPGLLTPPVATELSQNARHLQGGGEKQRVF  
TGIVTSLHDYFGVVDEEVFFQLSVVKGRLPQLGEKVLVKAAYNPGQAVPWNNAVKVQTL  
SNQPLLKSPAPLLHVAALGQKQGILGAQPQLIFQPHRIPPLFPQKPLSLFQTSHTLHLS  
HLNRFPARGPHGRDLQGRSDDYDSKKRKQRAGGEPWGAKKPRHDLPPYRVHLTPYT  
VDSPICDFLELQRRYRSLLVPSDFLSVHLSWLSAFPLSQPFSLHHP SRIQVSSEKEAAPD  
AGAEPITADSDPAYSSKVLLLSSPGLEELYRCCMLFVDDMAEPRETPEHPLKQIKFLLGR  
KEEEAVLVGGEWSPSLDGLDPQADPQVLVRTAIRCAQAQTGIDLSGCTKWWRFAEFQ

YLQPGPPRRLQTVVVYLPDVWTIMPTLEEWEALCQQKAAEAAPPTQEAQGETEPTTEQA  
 PDALEQAADTSRRNAETPEATTQQETDLDLPEAPPPLEPAVIARPGCVNLSLHGIVED  
 RRPKERISFEAGVMVLAELFLEMLQRDFGYRVYKMLLSLPEKVVSPPEPEKEEAAKEEA  
 TKEEEAIKEEVVKEPKDEAQNENGPATESEAPLKEDGLLPKPLSSGEEEEEEKPRGEASED  
 LCEMALDPELLLLRRDDGEEEFAGAKLEDSEVRSVASNQSEMEFSSLQDMPKELDPSAV  
 LPLDCLLAFVFFDANWCGYLHRRDLERILLTLGIRLSAEQAKQLVSRVVTQNICQYRSLQ  
 YSRQEGLDGGLPEEVLFGNLDLLPPPGKSTKPGAAPTEHKALVSHNGSLINVGSLQLQRA  
 EQQDSGRLYLENKIHTLELKLEESHNRFSATEVTNKTAAEMQELRVRLAEAEETARTA  
 ERQKSQQLRLLQELRRRLTPQLEIQRVVEKADSWVEKEEPAPSN

SEQID No:54

MAPIGLKAVVGEKIMHDEVKVKKKGEWKVLVVDQLSMRMLSSCCKMTDIMTEGITED  
 INKRREPLPSLEAVYLITPSEKSVHSLISDFKDPPTAKYRAAHVFFTDSCPDALFNELVKS  
 RAAKVIKTLTEINIAFLPYESQVYSLDSADSFQSFYSPHKAQMKNPILERLAEQIATLCATL  
 KEYPAVRVRYGEYKDNALLAQLIQDKLDAYKADDPTMGEGPDKARSQLLILDRGFDPSPP  
 VLHELTFQAMSYDLLPIENDVYKYETSGIGEARVKEVLLDEDDDLWIALRHKHIAEVSQE  
 VTRSLKDFSSSKRMNTGEKTTMRDLSQMLKKMPQYQKELSKYSTHLHLAEDCMKHYYQ  
 GTVDKLCRVEQDLAMGTDAEGEKIKDPMRAIVPILLDANVSTYDKIRIILLYIFLKNGITEE  
 NLNKLIIQHAQIPPEDSEIITNMAHLGVPIVTDSTLRRRSKPERKERISEQTYQLSRWTPIIK  
 DIMEDTIEDKLDTKHYPYISTRSSASFSTTAVSARYGHWKKNKAPGEYRSGPRLIIFILGG  
 VSLNEMRCAYEVTQANGKWEVLIGSTHILTPTKFLMDLRHPDFRESSRVSFEDQAPTM  
 E

SEQID No:55

VAGVRPSSPHGLVGAVSVGGAGVMAVETLSPDWEFDRVDDGSQKIHAQVQLKNYGGKF  
 LEEYTSQLRRIEDALDDSIGDVWDFNLDPIALKLLPYEQSSLELIKENTKVLNKVITVYAA  
 LCCEIKKLKYEAEATKFYNGLLFYGEGATDASMVEGDCQIQMGRFISFLQELSCFVTRCY  
 EVVMNVVHQLAALYISNKIAPKIIETTGVHFGTMYEHLGELLTVLLTLDEIIDNHITLKDHW  
 TMYKRLLKSVHHNPSKFGIQEEKLPFEKFLKLEGQLLDGMIFQACIEQQFDSLNGGVS  
 VSKNSTFAEEFAHSIRSIFANVEAKLGEPSEIDQRDKYVGICGLFVLHFQIFRTIDKKFYKS  
 LLDICKKVPAILTANIIWFPDNFLIQIPAAAKLLDRKSLQAIIHRDFTLQQKAQSLTKDV  
 QSYVVFVSSWMMKMESILSKEQRMDKFAEDLTNRCNVFIQGFYAYSISTIIKTMMNLYM  
 SMQKPMTKTSVKALCRLVELLKAIEHMFYRRSMVVADSVSHITQHLQHQAALHSISVAKK  
 RVISDKKYSEQRLDVLSALVLAENTLNGPSTKQRRRLIVSLALSVGTQMKTFFKDEELFPLQ

VVMKKLDLISELRERVQTQCDCCFLYWHRAVFPIYLDDVYENAVDAARLHYMFSA LRDC  
 VPAMMHARHLESYEILLDCYDKEIMEILNEHLLDKLCKEIEKDLRLSVHTHLKLDDRNPFK  
 VGMKDLALFFSLNPIRFFNRFIDIRAYVTHYLDKTFYNLTVALHDWATYSEMRNLATQR  
 YGLVMTEAHLPSQTLEQGLDVLEIMRNIHIFVSRYLYNLNNQIFIERTSNNKHLNTINIRHI  
 ANSIRTHGTGIMNTTVNFTYQFLKKKFYIFSQFMYDEHIKSRLIKDIRFFREIKDQNDHKY  
 PFDRAEKFNRGIRKLGITPEGQSYLDQFRQLISQIGNAMGYVRMIRSGGLHCSSNAIRFV  
 PDLEDIVNFEELVKEEGLAEETLKAARHLDSVLSDHTRNSAEGTEYFKMLVDVFAPEFR  
 RPKNIHLRNFYIIVPPLTLNFVEHSISCKEKLNNKKNIGAAFTDDGFAMGVAYILKLLDQYR  
 EFDLHWQSVREKYLKEIRAVAKQQNVQSASQDEKLLQTMNLTQKRLDVYLQEFELL  
 YFSLSSARIFFRADKTAAEENQEKEKEEETKTSNGDLSDSTVSADPVVK

SEQID No:56

MRLKLFSILSTALLRATDTINSQGQFPSYLETVTKDILAPNLQWHAGRTAAAIRTA AVSCL  
 WALTSSSEVLSAEQIRDVQETLMPQVLTLEEDSKMTRLISCRINTFLKTSGGMTDPEKLI  
 KIYPELLKRLDDVSNDVRMAAASLTVLWLQCVKGANAKSYYQSSVQYLYRELLVHLDDP  
 ERAIQDAILEVLKEGSGLFPDLLVRETEAVIHKHRSATYCEQLLQHVQAVPATQ

SEQID No:57

MRNLKLFRTLEFRDIQGPNGPQCFSRLRTEQGTVLIGSEHGLIEVDPVSREVKNEVSLVA  
 EGFLPEDGSGRIVGVQDLLDQESVCVATASGDVILCSLSTQQLECVGGSVASGISVMSW  
 SPDQELVLLATGQQTLIMMTKDFEPILQQIHQDDFGESKFITVGWGRKETQFHGSEGR  
 QAAFQMQMHESALPWDDHRPQVTWRGDGQFFAVSVVCPETGARKVRVWNREFALQ  
 STSEPVAGLGPALAWKPSGSLIASTQDKPNQQDIVFFEKNGLLHGHFTLPFLKDEVKVN  
 DLLWNADSSVLAVRLEDLQREKSSIPKTCVQLWTVGNYHWYLKQSLSFSTCGKSKIVSL  
 MWDPVTPYRLHVLCCQGWHLAYDWHWTDRSVGDNSSDLNVAVIDGNRVLVTVFR  
 QTVVPPPMCTYQLLFPHPVNQVTFLAHPQKSNLDASNQISVYKCGDCPSADPTV  
 KLGAVGGSGFKVCLRTPHLEKRYKIQFENNEDQDVNPLKLGLLTWIEEDVFLAVSHSEF  
 SPRSVIHHLTAASSEMDEEHGQLNVSSSAAVDGVIIISLCCNSKTKSVVLQLADGQIFKYL  
 WESPSLAIKPWKNSSGGFPVRFPYPCTQTELAMIGEEECVLGLTDRCRFFINDIEVASNIT  
 SFAVYDEFLLLTTHSHTCQCFCRLDASFCTLQAGLSSNHVSHGEVLRKVERGSRIVTVV  
 PQDTKLVLQMPRGNLEVHHRALVLAQIRKWLDKLMFKEAFECMRKLRINLNPIYDHNP  
 KVFLGNVETFIKQIDSVNHINLFFTELKEEDVTKTMYAPVTSSVYLSRDPDGNKIDLVCD  
 AMRAVMESINPHKYCLSILTSHVKKTTPELEIVLQKVHELQGNAPSDPDVSAEEALKYL  
 LHLVDVNELYDHSLGTYDFDLVLMVAEKSQKDPKEYLPFLNTLKKMETNYQRFTIDKYL

KRYEKAIGHLSKCGPEYFPECLNLIKDKNLYNEALKLYSPSSQQYQDISIAYGEHLMQEH  
 MYEPAGLMFARCGAHEKALSAFLTTCGNWKQALCVAQAQLNFTKDQLVGLGRTLAKGLV  
 EQRKHIDAAMVLEESAQDYEEAVLLLLLEGAAWEEALRLVYKYNRLDIETNVKPSILEAQ  
 KNYMAFLDSQTATFSRHKKRLLVVRELKEQAQQAGLDDEVPHGQESDLFSETSSVVS  
 SEMSGKYSHSNSRISARSSKNRRKAERKKHSLKEGSPLEDLALLEALSEVVQNTENLKD  
 EVYHILKVLFLFEFDEQGRELQKAFEDTLQLMERSLPEIWTLYQQNSATPVLGPNSTAN  
 SIMASYQQQKTSVPVLDALFIPPKINRRTQWKLSLLD

SEQID No:58

MVQKKKFCPRLLDYLIVGARHPSSDSVAQTPELLRRYPLEDHTEFPLPPDVVFFCQPE  
 GCLSVRQRRMSLRDDTSFVFTLTDKDTGVTRYGICVNFYRSFQKRISKGKGEGGAGSR  
 GKEGTHATCASEEGGTESSESGLQPFSAADSTPDVNQSPRGKRRAKAGSRSRNSTL  
 TSLCVLSHYPPFFSTFRECLYTLKRLVDCCSERLLGKKLGIPRGVQRDTMWRIFTGSLLVE  
 EKSSALLHDLREIEAWIYRLLRSPVPVSGQKRVDIEVLPQELQPALTFALPDPSRFTLVDF  
 PLHLPLELLGVDACLQLLTCILLEHKVVLQSRDYNALSMSVMAFVAMIYPLEYMFPVIPL  
 PTCMASAEQLLLAPTPYIIGVPASFFLYKLDFKMPDDVWLVDLDSNRVIAPTNAEVLPI  
 EPESLELKKHLKQALASMSLNTQPILNLEKFHEGQEIPLLLGRPSNDLQSTPSTEFNPLIY  
 GNDADSDVDVATRVAMVRFFNSANVLQGFQMHTRTLRLFP RPVVAFAQGSFLASRPRQ  
 TPFAEKLARTQAVEYFGEWILNPTNYAFQRIHNNMFDPALIGDKPKWYAHQLQPIHYRV  
 YDSNSQLAEALSVPPPERDSDSEPTDDSGSDSMDYDDSSSSYSSLGDFVSEMMKCDIN  
 GDTPNVDPLTHAALGDASEVEIDELQNQKEAEPEGPDSENSQENPPLRSSSSTTASSS  
 PSTVIHGANSEPADSTEMDDKAAVGVSKPLPSVPPSIGKSNVDRRQAEIGEGSVRRRIY  
 DNPYFEPQYGFPPPEEDEDQGESYTPRFSQHVSNGNRAQKLLRPNSLRLASDSDAESD  
 SRASSPNSTVSNTSTEGFGGIMSFASSLYRNHSTSFSLSNLTLPTKGAREKATPFPSLK  
 VFGLNTLMEIVTEAGPGSGEGNRRALVDQKSSVIKHSPTVKREPPSPQGRSSNSSENQ  
 QFLKEVVHSLVDGQGVGWLNMKKVRRLLLESEQLRVFVLSKLNRMVQSEDDARQDIIPD  
 VEISRKVYKGMLDLLKCTVLSLEQSYAHAGLGGMASIFGLLEIAQTHYYSKEPDKRKRSP  
 TESVNTVPVGKDPGLAGRGDPKAMAQLRVPQLGPRAPSATGKGPKELDTRSLKEENFIA  
 SIELWNKHQEVKKQKALEKQRPEVIKPVFDLGETEEKKSQISADSGVSLTSSSQRTDQD  
 SVIGVSPAVMIRSSSQDSEVSTVVSNSSETLGADSDLSSNAGDGPGGEGSVHLASSR  
 GTLSDSEIETNSATSTIFGKAHSLKPCIKEKLAGSPIRTSEDVSQRVLYEGLLGRDKGS  
 MWDQLEDAAMETFSISKERSTLWDQMQFWEDAFLDAVMLEREGMGMDQGPQEMIDR  
 YLSLGEHDRKRLEDDEDRLATLLHNLISYMLLMKVKNKNDIRKKVRRMLMGKSHIGLVYSQ  
 QINEVLDQLANLNGRDLSIWSSGSRHMKKQTFVVHAGTDTNGDIFFMEVCDDCVLRS

NIGTVYERWWYEKLINMTYCPKTKVLCLWRRNGSETQLNKFYTKKCRELYYCVKDSME  
RAAARQQSIKPGPELGGEFPVQDLKTGEGGLLQVTLEGINLKFMHNQVFIELNHIKKCNT  
VRGVFVLEEFVPEIKEVVSHKYKTPMAHEICYSVLCFSYVAAVHSSEEDLRTPPRPVSS

SEQID No:59

AAASRCPGIMVALRGLGSGLQPWCPLDLRLEWVDTVWELDTETEPDPSIEAEIETGL  
AAFTKLYESLLPFATGEHGSMESIWTFFIENNVSHSTLVALFYHFVQIVHKKNVSVQYRE  
YGLHAAGLYFLLLEVPGSVANQVFHPVMFDKCIQTLKKSWPQESNLNRKRKKEQPKSS  
QANPGRHRKRKGKPPRRREDIEMDEIEEQEDENICFSARDLSQIRNAIFHLLKNFLRLLPKF  
SLKEKPQCVCQNCIEVFVSLTNFEPVLHECHVTQARALNQAKYIPELAYYGLYLLCSPHIG  
EGDKVISCVFHQMLSVILMLEVGEGSHRAPLAVTSQVINCRNQAVQFISALVDELKESIF  
PVVRILLQHICAKVVDKSEYRTFAAQSLVQLLSKLPCEYAMFIAWLYKYSRSSKIPHRV  
FTLDVVLALLELPEREVDNTLSLEHQKFLKHKFLVQEIMFDRCLDKAPTVRSKALSSFAH  
CLELTVTSASESILELLINSPTFSVIESHPGTLLRNSSAFSYQRQTSNRSEPSGEINIDSSG  
ETVGSGGERCVMAMLRRIIRDEKTNVRKSALQVLVSILKHCDVSGMKEDLWILQDQCRD  
PAVSVRKQALQSLTELLMAQPRCVQIQKAWLRGVVPVMDCESTVQEKALEFLDQLLL  
QNIRHHSHFHSGDDSQVLAWALLTLLTTESQELSRYLNAFHIWSKKEKFSPTFINNVIS  
HTGTEHSAPAWMLLSKIAGSSPRLDYSRIIQSWEKISSQQNPNSNTLGHILCVIGHIAKHL  
PKSTRDKVTDVAVKCKLNGFQWSLEVISSAVDALQRLCRASAETPAEEQELLTQVCGDV  
LSTCEHRLSNIVLKENG TGNMDEDLLVKYIFTLG DIAQLCPARVEKRIFLLIQSVLASSAD  
ADHSPSSQGSSEAPASQPPPQVRGSMPSVIRAHAIITLGKLCQHEDLAKKSIPALVRE  
LEVCEDVAVRNNVIIVMCDLCIRYTIMVDKYIPNISMCLKDSDPFIRKQTLILLTNLLQEEFV  
KWKGSLFFRFVSTLIDSHPDIA SFGEFCLAHLLLKRNPVMFFQHFI ECIFHFNNYEKHEKY  
NKFPQSEREKRLFSLKGKSNKERRMKIYKFLLEHFTDEQRFNITSKICLSILACFADGILPL  
DLDASELLSDTFEVLSSKEIKLLAMRSKPKDLLMEEDDMALANVVMQEAQKKLISQVQ  
KRNFIENIIPIIISLKT VLEKNKIPALRELMHYLREVMQDYRDELKDFFAVDKQLASELEYD  
MKKYQEQLVQEQLAKHADVAGTAGGAEVAPVAQVALCLETVPVPAGQENPAMSPAV  
SQPCTPRASAGHVAVSSPTPETGPLQRLLPKARPM SLSTIAILNSVKKAVESKSRHRSR  
SLGVLPFTLN S GSPEKTC SQVSSYSLEQESNGEIEHVTKRAISTPEKSISDVTFGAGVSYI  
GTPRTPSSAKEKIEGRSQGNDILCLSLPDKPPPQQQWNVRSPARNKDTPACSRRSLR  
KTPLKTAN

SEQID No:60

MWNDIELLTNDDTGSGYLSVGSRKEHGTALYQVDLLVKISSEKASLNPKIQACSLSDGFI

IVADQSVILLDSICRSLQLHLVFDTEVDVVGLCQEGKFLLVGERSGNLHLIHVTSKQTLT  
 NAFVQKANDENRRTYQNLVIEKDGSNEGTYMMLLLTYSGFFCITNLQLLKIQAIEENVDF  
 STAKKLQGQIKSSFISTENYHTLGCLSLVAGDLASEVPVIIGGTGNCAFSKWEPDSSKKG  
 MTVKNLIDAEIIGGAKKFQLIDNLLFVLDTDNVLSLWDIYTLTPVWNWPSLHVEEFLLTTE  
 ADSPSSVTWQGITNLKLIALTASANKKMKNLMVYSLPTMEILYSLEVSSVSSLVQTGISTD  
 TIYLLEGVCKNDPKLSEDSVSVLVLRLCLTEALPENRLSRLHKKHRFAEAESFAIQFGLDV  
 ELVYKVKSNIHLEKLALSSVDASEQTEWQQLVDDAKENLHKIQDDEFVNYCLKAQWIT  
 YETTQEMLNIAKTRLLKKEDKTALIYSDGLKEVLRAHAKLTTFYGAFGPEKFSGSSWIEF  
 LNNEDDLKDIFLQLKEGNLVCAQYLWLRHRANFESRFDVKMLESLLNSMSASVSLQKLC  
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SEQID No:61

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SEQID No:62

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SEQID No:63

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SEQID No:64

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SEQID No:65

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SEQID No:66

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SEQID No:67

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 ASSGSLDDTEMEQLLQEEQSECSSVHTAATPERRGSLPDTGWKHERKLSSSESQV

SEQID No:68

MRRAPCVRDKLREIVGASTNWRDHVKAMEERKLLHSFLAKSQDGLPPRRMKDSYIEVL  
 LPLGSEPELREKYLTQNTVRFGRILEDLDLGLVLCYMHNKIHSKMSPLSIVTALVDKI  
 DMCKKSLSPEQDIKFSGHVSWSVGKTSMEVKMQMFQLHGDEFPCVLDATFVMVARDSE  
 NKGPAFVNPLIPESPEEEELFRQGELNKGRRIAFSSTSLKMAPSAEERTTIHEMFLSTL  
 DPKTISFRSRVLPSNAVWMENSKLKSLEICHQPERNIFNRIFGGFLMRKAYELAWATAC  
 SFGGSRPFVVAVDIMFQKPVEVGSLLFLSSQVCFTQNNYIQVRVHSEVASLQEKQHTT  
 TNVFHFTFMSEKEVPLVFPKTYGESMLYLDGQRHFNSMSGPATLRKDYLVEP

SEQID No:69

MSVKEAGSSGRREQAAYHLHIYPQLSTTESQASCRVTATKDSTTSQVIKDAIASRLDG  
 TKCYVLVEVKESGGEEWVLDANDSPVHRVLLWPRAAQDEHPQEDGYFLLQERNADG  
 TIKYVHMQLVAQATATRRRLVERGLLPRQQADFDLCLNLPTELTEGNLLKNLKHRFLQQKI  
 YTYAGSILVAINPFKFLPIYNPKYVKMYENQQLGKLEPHVFALADVAYYTMLRKRNVNCCI  
 VYPGESGSGKTQSTNFLIHCLTALSQKGYASGVERTILGACPVLEAFGNAKTAHNNNSS  
 RFGKFIQVSYLESGIVRGAVVEKYLLEKSRLVSQEKDERNYHVFFYLLLVSEEEERQEF  
 QLKQPEDYFYLNQHNLIKIEDGEDLKHDFERLQAMEMVGFLPATKKQIFAVLSAILYLGN  
 VTYKKRATGREGLEVGPPEVLDLTSQLLKVKREILVEVLTKRKTVTVNDKLILPYSLSEA  
 ITARDSMAKSLYSALFDWIVLRINHALLNKKDVEEAVSCLSIGVLDIFGFEDFERNSEFQF  
 CINYANEQLQYYFNQHIFKLEQEEYQGEGITWHNIGYTDNVGCIHLISKKPTGLFYLLDEE  
 SNFPHATSQTLLAKFKQQHEDNKYFLGTPVMEPAFIIQHFAGKVYQIKDFREKNMDYM  
 RPDIVALLRGSDSSYVRELIGMDPVAVFRWAVLRRAAIRAMAVLREAGRLRAERAEGAAG  
 MSSPGAQSHPEELPRGASTPSEKLYRDLHNQMIKSIKGLPWQGEDPRSLQLSLSRLQK

PRAFILKSKGIKQKQIIPKNLLDSKSLKLIISMTLHDRTTKSLLHLHKKKKPPSISAQFQTSL  
 NKLEALGKAEPFFIRCIRSNAEKKELCFDDELVLQQLRYTGMLTVRIRRSYGYSKYTF  
 QDFTEQFQVLLPKDAQPCREVISTLLEKMKIDKRNYQIGKTKVFLKETERQALQETLHRE  
 VVRKILLQSWFRMVLERRHFLQMKRAAVTIQACWRSYRVRRALERTQAAVYLQAAWR  
 GYWQRKLYRHQKQSIIRLQSLCRGHLQRKSFSQMISEKQKAEEKEREALEAARAGAE  
 GGQQAAGGQQVAEQGPEPAEDGGHLASEPEVQPSDRSPLEHSSPEKEAPSPEKTL  
 PPQKTVAAESHEKVPSSREKRESRRQRGLEHVKFQNKHIQSCKEESALREPSRRVTQE  
 QGVSLLEDKKESREDETLVETEAEANTSQKQPTEQPQAMAVGKVSEETEKTLPSGSP  
 RPGQLERPTSLALDSRVSPAPGSAPETPEDKSKPCGSPRVQEKPDSPGGSTQIQRYL  
 DAERLASAVELWRGKKLVAAASPSAMLSQSLDLSDRHRATGAALTPTEERRTSFSTSD  
 VSKLLPSLAKAQPAEETDGERSAKKPAVQKKKPGDASSLPDAGLSPGSQVDSKSTFK  
 RLFLHKTCDKKYSLEGAELENAVSGHVLEATTMKKGLEAPSGQQHRHAAGEKRTKE  
 PGGKGKKNRNVKIGKITVSEKWRESVFRQITNANELKYLDEFLLNKINDLRSQKTPIESLF  
 IEATEKFRSNIKTMYSPNGKIHVGYKDLMENYQIVVSNLATERGQKDTNLVLNLFQSL  
 DEFTRGYTKNDFEPVKQSKAQKKKRKQERAVQEHNGHVFAZYQVSIPQSCEQCLSYIW  
 LMDKALLCSVCKMTCHKCVHKIQSHCSYTYGRKGEPGAEPGHFGVCVDSLTSKASV  
 PIVLEKLEHVEMHGLYTEGLYRKSGAANRTRELRLQALQTDPAAVKLENFPIHAITGVLK  
 QWLRELPEPLMTFAQYGDFLRAVELPEKQEQLAAIYAVLEHLPEANHNSLERLIFHLVKV  
 ALLEDVNRMSPGALAIIFAPCLLRCPDNSDPLTSMKDVLKITTCVEMLIKEQMRKYKVKM  
 EESISQLEAAESIAFRRLSLLRQNANKSPKTREPAGGAGRLLTTSRVSPSPSTRNLALGS  
 WRSAALRTRGTGRPARPGRARALRRRPPRPAPRESPAQPPRSRPRVRTETPSPLSSGP  
 PPSRSNTGMAPLRR

SEQID No:70

MTGERPSTALPDRRWGPRILGFWGGCRVWVFAAIFLLLSLAASWSKAENDFGLVQPLV  
 TMEQLLWVSGRQIGSVDTFRIPITATPRGTLFAFAEARKMSSSDEGAKFIALRRSMDQ  
 GSTWSPTAFIVNDGDVPDGLNLGAVVSDVETGVVFLFYSLCAHKAGCQVASTMLVWSK  
 DDGVSWSTPRNLSLDIGTEVFAPGPGSGIQKQREPRKGR LIVCGHGTLERDGVFCLLS  
DDHGASWRYGSGVSGIPYGQPKQENDFNPDECQPYELPDGSVINARNQNNYHCHC  
 RIVLRSYDACDTRLRPRDVTFDPELVDPVVAAGAVVTSSGIVFFSNPAHPEFRVNLTLRW  
 SFSNGTSWRKETVQLWPGPSGYSSLATLEGSMDEEQAPQLYVLYEKGRNHYTESIS  
 VAKISVYGTL

SEQID No:71

MAPRLCSISVTARRLLGGPGPRAGDVASAAAARFYSKDNEGSWFRSLFVHKVDPRKDA  
 HSTLLSKKETSONLYKIQFHNVKPEYLDAYNSLTEAVLPKLHLDDEYPCSLVGNWNTWYG  
 EQDQAVHLWRFSGGYPALMDCMNKLKNNKEYLEFRRERSQMLLSRRNQLLLEFSFWN  
 EPQPRMGPNIELRTYKLKPGTMIEWGNNWARAIKYRQENQEAVGGFFSQIGELYVVH  
 HLWAYKDLSREETRANAARWRKRGWDENVYYTVPLVRHMESRIMIPLKISPLQ

SEQID No:72

MAARVLRARGAAWAGGLLQRAAPCSLLPRLRTWTSSSNRSREDSWLKSLFVRKVDPR  
 KDAHSNLLAKKETSONLYKLQFHNVKPECLEAYNKICQEVLPKIHEDKHYPCTLVGTWNT  
 WYGEQDQAVHLWRYEGGYPALTEVMNKLRENKEFLEFRKARSDMLLSRKNQLLLEFS  
 FWNPEVPRSGPNIELRSYQLRPGTMIEWGNYWARAIRFRQDGNEAVGGFFSQIGQLY  
 MVHHLWAYRDLQTREDIRNAAWHKHGWEELVYYTVPLIQEMESRIMIPLKTSPLQ

SEQID No:73

MGTALLQRGGCFLCLSLLLLGCWAELGSGLEFPGAEGQWTRFPKWNACCSEMSFQ  
 LKTRSARGLVLYFDDEGFCDLFLELILTRGGRLQLSFSIFCAEPATLLADTPVNDGAWHSV  
 RIRRQFRNTTLFIDQVEAKWVEVKSKRRDMTVFSGLFVGGLPPELRAAALKLTLASVRE  
 REPFKGWIRDVRVNSSQVLPVDSGEVKLDDEPPNSGGGSPCEAGEEGEGGVCLNGG  
 VCSVDDQAVCDCSRTGFRGKDCSQEDNNVEGLAHLMMGDQGKSKGKEEYIATFKG  
 SEYFCYDLSQNPIQSSSDEITLSFKTLQRNGLMLHTGKSADYVNLALKNGAVSLVINLGS  
 GAFEALVEPVNGKFNDNAWHDKVTRNLRQHSGIGHAMVTISVDGILTTTGYTQEDYT  
 MLGSDDFFYVGGSPSTADLPGSPVSNNFMGCLKEVVYKNNDVRLELSRLAKQGDPKM  
 KIHGVVAFKCNVATLDPITFETPESFISLPKWNAKKTGSISFDFRTTEPNGLILFSHGKP  
 RHQKDAKHPQMIKVDFFAIEMLDGHLYLLLDMGSGTIKIKALLKKVNDGEWYHVDQFQD  
 GRSGTISVNTLRTPYTAPGESEILDLDDELYLGGLPENKAGLVFPTEVWTALLNYGYVG  
 CIRDLFIDGQSKDIRQMAEVQSTAGVKPSCSKETAKPCLSNPCKNNGMCRDGNRYV  
 CDCSGTGYLGRSCEREATVLSYDGSFMFKIQLPVVMHTEAEDVSLRFRSQRAYGILMA  
 TTSRDSADTLRLELDAGR~~V~~KLTVNLDCIRINCNSSKGPETLFAGYNLNDNEWHTVRVVR  
 RGKSLKLTVDQDQAMTGQAGDHTRLEFHNIETGIITERRYLSVSPSNFIGHLQSLTFN  
 GMAYIDLCKNGDIDYCELNARFGFRNIIADPVTFKTKSSYVALATLQAYTSMHLFFQFQT  
 TSLDGLILYNSGDGNDFIVVELVKGYLHYVFDLGNANLIKSSNKPLNDNQWHNVMIS  
 RDTSNLHTVKIDTKITTQITAGARNLDLKSPLYGGVAKETYKSLPKLVHAKEGFQGCCLAS  
 VDLNGRLPDLISDALFCNGQIERGCEGPSTTCQEDSCSNQGVCLQQWDGFSDCDSMT

SFSGPLCNDPGTTYIFSKGGGQITYKWPPNDRPSTRADRLAIGFSTVQKEAVLVRVDSS  
 SGLGDYLELHIHQGKIGVKFNVTDDIAEESNAIINDGKYHVVRFTRSGGNATLQVDSW  
 PVIERYPAGRQLTIFNSQATIIIGGKEQGQPFQGGQLSGLYYNGLKVLNMAAENDANIAIVG  
 NVRLVGEVPSSMTTESTATAMQSEMSTSIMETTTTTLATSTARRGKPPTKEPISQTTDDIL  
 VASAECPSDDDEDIDPCEPSSGGLANPTRAGGREPYPGSAEVIRESSSTTGMVVGIVAAA  
 ALCILILLYAMYKYRNRDEGSYHVDESRNYISNSAQSNAGAVVKEKQPSSAKSSNKNKKN  
 KDKEYYV

SEQID No:74

MTTQQIDLQGGPWGFRVLVGGKDFEQPLAISRVTPGSKAALANLCIGDVITAIDGENTS  
 NMTHLEAQNRIKGCTDNLTLTVARSEHKVWSPLVTEEGKRHPYKMNLASEPQEV LHIG  
 SAHNRSAMPFTASPASSTTARVITNQYNNPAGLYSSENISNFNNALESKTAASGVEANS  
 RPLDHAQPPSSLVIDKESEVYKMLQEKLNEPPKQSTSFLVLQEILESEEKGDPNKPS  
 GFRSVKAPVTKVAASIGNAQKLPMCDKCGTGIVGVFVKLRDRHRHPECYVCTDCGTNL  
 KQKGHFFVEDQIYCEKHARERVTPPEGYEVVTVFPK

SEQID No:75

MGAGAETGRGQRAAAPERRHGRLLWLLRGLTLGTAPRRAVRGQAGGGGPGTAGIVG  
 EAGSLATCELPLAKSEWQKKLTPEQFYVTREKGTPEPPFSGIYLNKEAGMYHCVCCDS  
 PLFSSEKKYCSGTGWPSFSEAHGTSGSDESHTGILRRLDTSLSARTEVVCKQCEAHL  
 GHVFPDGPNGQRFCINSVALKFKPRKH

SEQID No:76

MTSAAPAKKPYRKAPPEHRELRLIPGSRLEQEEPLTDAERMKLLQEENEELRRRLASA  
 TRRTEALERELEIGQDCLELELGQSREELDKFKDKFRRLQNSYTASQRTNQELEDKLHT  
 LIKKAEMDRKTL DWEIVELTNKLLDAKNTINKLEELNERYRLDCNPAVQLLKCNKSHFRN  
 HKFADLPCELQDMVRKHLHSGQEAASPGPAPSLAPGAVVPTSVIARVLEKPESLLLNSA  
 QSGSAGRPLAEDVFVHVDMSSEGVP GDPASPPAPGSPTPQPNGECHSLGTARGSPEEE  
 LPLPAFEKLN PYPTPSPPHPLYPGRRVIEFSEDKVRIPRNSPLPNCTYATRQAISLSLVEE  
 GSERARPSVPSTPASAQASPHHQPSAPLTL SAPASSASSEEDLLVSWQRAFVD RTP  
 PPAVAQRTAFGRDALPELQRHFAHSPADRDEVVQAPSARPEESELLPTEPD SGFPR  
 EEEELNLPISPEEERQSLLPINRGTEEGPGTSHTEGRAWPLPSSSRPQRSPKRMGVHH  
 LHRKDSL TQAQEQGNLLN



SEQID No:77

MGTTASTAQQTVSAGTPFEGQLQGSGTMDSRHSVSIHSFQSTSLHNSKAKSIIPNKVAPV  
 VITYNCKEEFQIHDELLKAHYTLGRLSDNTPEHYLVQGRYFLVRDVTEKMDVLGTVGSC  
 GAPNFRQVQGGTLTVFGMGQPSLSGFRRVLQKLQKDGHRECVIFCVREEPVFLRADE  
 DFVSYTPRDKQNLHENLQGLGPGVRVESLELAIRKEIHDFACLSENTYHVYHNTEDLWG  
 EPHAVAIHGEDDLHVTEEVYKRPLFLQPTYRYHRLPLPEQGSPLAQLD AFVSVLRETP  
 SLLQLRDAHGPPPALVFSCQMVGVRTNLGMVLGTLILLHRSGTTSQPEAAPTQAKPLP  
 MEQFQVIQSFLRMVPQGRRMVEEVDRAITACAELHDLKEVVLENQKKLEGIRPESPAQ  
 GSGSRHSVWQRALWSLERYFYLLFNYYLHEQYPLAFALSFSRWLCAHPELYRLPVTLS  
 SAGPVAPRDLIARGSLREDDLVSPDALSTVREMDVANFRRVPRMPIYGT AQPSAKALG  
 SILAYLTD AKRRLRKVVVWSLREEAVLECDGHTYSLRWPGPPVAPDQLETLEAQLKAHL  
 SEPPPGKEGPLTYRFQTCLTMQEVFSQHRRACPLTYHRIPMPDFCAPREEDFDQLE  
 ALRAALSKDPGTGFVFSCLSGQGRTTAMVVAVLAFWHIQGFPEVGEELVSVPDAKF  
 TKGEFQVVMKVQQLPDGHRVKKEVDAALDTVSETMTPMHYHLREIIICTYRQAKAAKE  
 AQEMRRLQLRSLQYLERVCLILFNAYLHLEKADSWQRPFSTWMQEVASKAGIYEILNE  
 LGFPELESGEDQPFSRLRYRWQEQSCSLEPSAPEDLL

SEQID No:78

MAALYRPGLRLNWHGLSPLGWPSCRSIQTLRVLSGDLGQLPTGIRDFVEHSARLCQPE  
 GIHICDGTEAENTATLTLEQQGLIRKLPKYNNCWLARTDPKDVARVESKTVIVTPSQRD  
 TVPLPPGGARGQLGNWMSPADFQRAVDERFPGCMQGRMTMYVLPFSMGPVGSPLSRI  
 GVQLTDSAYVVASMRIMTRLGTPVLQALGDGDFVKCLHSGVQPLTGQGEVVSQWPCN  
 PEKTLIGHVPDQREIISFGSGYGGNSLLGKKCFALRIASRLARDEGWLAEHMLILGITSPA  
 GKALCAA AFPSACGKTNLAMMRPALPGWKVECVGDDIAWMRFDSEGRRLRAINPENG  
 FFGVAPGTSATTNP NAMATIQSNTIFTNVAETSDGGVYWEGIDQPLPPGVTVTSWLGP  
 WKPGDKEPCAHPNSRFCAPARQCPIMDPAWEAPEGVPIDAIIFGGRRPKGVPLVYEF  
 NWRHGVFVGRAMRSESTAAAEHKGKIIMHDPFAMRPFFGYNFGHYLEHWLSMEGRKG  
 AQLPRIFHVNWFRRDEAGHFLWPGFGENARVLDWICRRLEGEDSARETPIGLVPKEGA  
 LDLSGLRAIDTTQLFSLPKDFWEQEVDRDIRSYLTEQVNQDLPKEVLAELEALERRVHKM

SEQID No:79

MLPAATASLLGPLL TACALLPFAQGQTPNYTRPVFLCGGDVKGESGYVASEGFPNLYP  
 PNKECIWTITVPEGQTVSLSFRVFDLELHPACRYDALEV FAGSGTSGQRLGRFCGTFRP  
 APLVAPGNQVTLRMTTDEGTGGRGFLLWYSGRATSGTEHQFCGGRLEKAQGTLTTPN

WPESDYPPGISCSWHIIAPPDQVIALTFEKFDLEPDTYCRYDSVSVFNGAVSDDSRRLG  
KFCGDAVPGSISSEGNELLVQFVSDLSVTADGFSASYKTLPRGTAKEGQGPGRGTE  
PKVKLPPKSQPPEKTEESPSAPDAPTCPKQCRRTGTLQSNFCASSLVVTATVKSMVRE  
PGEGLAVTVSLIGAYKTGGLDLPSPPTGASLKFYVPCKQCPPMKKGVSYLLMGQVEEN  
RGPVLPPESFVVLHRPNQDQILTNL SKRKCPSPVRAAASQD

SEQID No:80

MRMTMEEMKNEAETTSMVSMPLYAVMYPVFNELERVNLSAAQTLRAAFIKA EKENPGL  
TQDIIMKILEKKSVEVNFTESLLRMAADDVEEYMIERPEPEFQALNEKARALKQILSKIPD  
EINDRVRFLQTIKDIASAIKELLDTVNNVFKKYQYQNRRALEHQKKEFVKYSKSFSDTLKT  
YFKD GKAINVFVSANRLIHQTNLILQTFKTVA

SEQID No:81

MTSALTQGLERIPDQLGYLVLSEGAVLASSGDLENDEQAASAISELVSTACGFRLHRGM  
NVPFKRLSGEPLPLPLVVVLGAGGYFQGLLG FSSSSLLPSPGVSGLATFLPLGLPGIRIV  
NEKARERRSSRGHSSSNL

SEQID No:82

MGSRDHLFKVLVVGDAAVGKTSLVQRYSQDSFSKHYKSTVGVD FALKVLQWSDYEIVR  
LQLWDIAGQERFTSMTRLYYRDASACVIMFDVTNATTFSNSQRWKQDLDSKLTLPNGE  
PVPCLLLANKCDLSPWAVSRDQIDRFSKENGFTGWTETSVKENKNINEAMRVLIEKMM  
RNSTEDIMSLSTQGDYINLQTKSSSWSCC

SEQID No:83

MAAAKDTHEDHDTSTENTDESNHDPQFEP IVSLPEQEIKTLEEDEEELFKMRAKLFRFA  
SENDLPEWKERTGTDVKLLKHKEKGAI RLLMRRDKTLKICANH YITPMMELKPNAGSDR  
AWVWNTHADFADEC PKPELLAIRFLNAENAQKF KTFEECRKEIEEREKKAGSGKNDH  
AEKVAEKLEALSVKEETKEDAE EKQ

SEQID No:84

MLDSSDSSSQPHWSNELIAEQLQQQVSQLQDQLDAELEDKRKV LLELSREKAQNEDLK  
LEV TNILQKHKQEV ELLQNAATISQPPDRQSEPATHPAVLQENTQIEPSEPKNQEEKLS  
QVLNELQVSHAETTLELEKTRDMLILQRKINVCYQEELEAMMTKADNDNRDHKEKLERL  
TRLLDLKNNRIKQLEGILRSHDLPTSEQLKDVAYGTRPLSLCLETLP AHGDEDKVDISLLH

QGENLFELHIHQAFLTSAALAQAGDTQPTTFCTYSFYDFETHCTPLSVGPQPLYDFTSQ  
 YVMETDSLFLHYLQEASARLDIHQAMASEHSTLAAGWICFDRVLETVEKVHGLATLIGA  
 GGEEFGVLEYWMRLRFPIKPSLQACNKRKKAQVYLSTDVLGGRKAQEEEFRRSESWEP  
 QNELWIEITKCCGLRSRWLGTQPSPYAVYRFFTFSDHDTAIIPASNNPYFRDQARFPVLV  
 TSDLDHYLRREALSIHVFDDEDLEPGSYLGRARVPLLPLAKNESIKGDFNLTDPAEKPNG  
 SIQVQLDWKFPYIPPESEFLKPEAQTKGKDTKDSSKISSEEEKASFPSQDQMASPEVPIEA  
 GQYRSKRKPPHGGGERKEKEHQVVSYSRRKHGKRIGVQGKNRMEYLSLNILNGNTPQQ  
 VNYTEWKFSETNSFIGDGFKNQHEEEEMTLSHSALKQKEPLHPVNDKESSEQGEVSE  
 AQTTDSDDVIVPPMSQKYPKADSEKMCIEIVSLAFYPEAEVMSDENIKQVYVEYKFYDLP  
 LSETETPVSLRKPRAGEEIHFFHFSKVIDLDPQEQQGRRRFLFDMLNGQDPDQGHKFTV  
 VSDPLDEEKKECEEVGYAYLQLWQILESGRDILEQELDIVSPEDLATPIGRLKVSLLQAAA  
 VLHAIYKEMTEDLFS

SEQID No:85

MERSGWARQTFLALLLGATLRARAAAGYYPRFSPFFFLCTHHGELEGDGEQGEVLISL  
 HIAGNPTYYPGQEYHVTISTSTFFDGLLVTGLYTSTSVQASQSIGGSSAFGFGIMSDHQ  
 FGNQFMCSVVASHVSHLPTTNLSFIWIAPPAGTGCVNFMATATHRGQVIFKDALAQQLC  
 EQGAPTDVTVHPLAEIHSDSIILRDDFDSYHQLQLNPNIWVECNNCETGEQCGAIMHG  
 NAVTFCEPYGPRELITTGLNTTTASVLQFSIGSGSCRFSYSDPSIIVLYAKNNSADWQLE  
 KIRAPSNVSTIIHILYLPEDAKGENVQFQWKQENLRVGEVYEACWALDNILIINSAHRQVV  
 LEDSLDPVDTGNWLVFFPGATVKHSCQSDGNSIYFHGNEGSEFNFATTRDVDLSTEDIQ  
 EQWSEEFESQPTGWDVLGAVIGTECGTIESGLSMVFLKDGERKLCTPSMDTTGYGNLR  
 FYFVMGGICDPGNSHENDIILYAKIEGRKEHITDLSYSSYKVPSLVSVVINPELQTPATK  
 FCLRQKNHQGHNRNVWAVDFFHVLPLVLPSTMISHMIQFSINLGCGTHQPGNSVSLEFST  
 NHGRSWSLLHTECLPEICAGPHLPHSTVYSSENYSGWNRITIPNAALTRNTRIRWRQ  
 TGPILGNMWAIDNVYIGPSCCLKFCSGRGQCTRHGCKCDPGFSGPACEMASQTFPMFIS  
 ESFGSSRLSSYHNFYSIRGAEVSGCGVLASGKALVFNKEGRRQLITSFLDSSQSRFLQ  
 FTLRLGSKSVLSTCRAPDQPGEGVLLHYSYDNGITWKLLEHYSYLSYHEPRIISVELPGD  
 AKQFGIQFRWWQPYHSSQREDVWAIDEIIMTSVLFNSISLDFTNLVEVTQSLGFYLGNV  
 QPYCGHDWTLCTFTGDSKLASSMRYVETQSMQIGASYMIQFSLVMGCGQKYTPHMDN  
 QVKLEYSTNHGLTWHLVQEECLPSMPSCQEFTSASIYHASEFTQWRRVIVLLPQKTWS  
 SATRFRWSQSYTAQDEWALDSIYIGQQCPNMCSGHGSCDHGICRCDQGYQGTECH  
 PEAALPSTIMSDFENQNGWESDWQEVIGGEIVKPEQGCGVISSGSSLYFSKAGKRQLV  
 SWDLDTSWVDFVQFYIQIGGESASCNKPDSSREEGVLLQYSNNGGIQWHLLAEMYFSDF

SKPRFVYLELPAAAKTPCTRFRWWQPVFSGEDYDQWAVDDIILSEKQKQIIPVINPTLP  
 QNFYEKPAFDYPMNQMSVWLMLANEGMVKNETFCAATPSAMIFGKSDGDRFAVTRDL  
 TLKPGYVLQFKLNIGCANQFSSTAPVLLQYSHDAGMSWFLVKEGCYPASAGKGCEGNS  
 RELSEPTMYHTGDFEEWTRITIVIPRSLASSKTRFRWQIESSSQKNVPPFGLDGVYISEP  
 CPSYCSGHGDCISGVCFCDLGYTAAQGTCVSNVPHNEMFDRFEGKLSPLWYKITGA  
 QVGTGCGTLNDGKSLYFNPGPKREARTVPLDTRNIRLVQFYIQIGSKTSGITCIKPRTRN  
 EGLIVQYSNDNGILWHLLRELD FMSFLEPQIISIDLPQDAKTPATAFRWWQPQHGHKHA  
 QWALDDVLIGMNDSSQTGFQDKFDGSIDLQANWYRIQGGQVIDDCLSM TALIFTENIG  
 KPRYAETWDFHVSASTFLQFEMSMGCSKPFSSNSHSVQLQYSLNNGKDWHLVTEECVP  
 PTIGCLHYTESSITSERFQNWKRITVYLPLSTISPRTRFRWQIANYTVGADSWAIDNVVL  
 ASGCPWMCSGRGICDAGRCVCDRGFGGPYCVPVVPLPSILKDDFNGNLHPDLWPEVY  
 GAERGNLNGETIKSGTSLIFKGEGLRMLISRDLDCTNTMYVQFSLRFIAKSTPERSHSILL  
 QFSISGGITWHLMDDEFYFPQTTNILFINVPLPYTAQTNATRFRLWQPYNNGKKEEIWVD  
 DFIIDGNNVNNPVMLLDTFDFGPREDNWWFFYPGGNIGLYCPYSSKGAPEEDSAMVFVS  
 NEVGEHSITTRDLNVNENTI IQFEINVG CSTDSSSADPVRLEFSRDFGATWHLLLPLCYH  
 SSSHVSSLCSTEHHPSSTYYAGTMQGWRRREV VHFGLHLGCSVRFRWYQGFYPAGS  
 QPVTWAIDNVYIGPQCEEMCNGQGSCINGTKCICDPGYSGPTCKISTKNPDFLKDDFEG  
 QLESDRFLMSGGKPSRKCGILSSGNLFFNEDGLRMLMTRDLDLSHARFVQFFMRLG  
 CGKGVDPDRSQPVLLQYSLNGLSW SLLQEFLFSNSSNVGRYIALEIPLKARSGSTRLR  
 WWQPSENGHFYSPWVIDQILIGGNISGNTVLEDDFTTLD SRKWLLHPGGTKMPVCGST  
 GDALVFIEKASTRYVVSTDVAVNEDSFLQIDFAASC SVTDCSYAIELEYSVDLGLSWHPL  
 VRDCLPTNVECSRYHLQRILVSDTFNKWTRITLPLPPYTRSQATRFRWHQPAPFDKQQ  
 TWAIDNVYIGDGCIDMCSGHGRCIQGNCVCDEQWGGLYCDDPETS LPTQLKDNFNRA  
 PSSQNWLTVNGGKLSTVCGAVASGMALHFGSGGCSRLLVTVDLNL TNAEFIQFYFMYGC  
 LITPNNRNQGV LLEYSVNGGITWNLLMEIFYDQYSKPGFVNILLPPDAKEIATRFRWWQP  
 RHDGLDQNDWAIDNV LISGSADQRTVMLDTFSSAPVPQHERSPADAGPVGRIAFDMFM  
 EDKTSVNEHWLFHDDCTVERFCDSPDGVMLCGSHD GREVYAVTHDLTPTEGWIMQFK  
 ISVGCKVSEKIAQNIHVQYSTDFGVSWNYLVPQCLPADPKCSGSVSQPSVFFPTKGW  
 KRITYPLPESLVGNPVRRFRFYQKYSDMQWAIDNFYLGPGCLDNCRGHGDCLREQCICD  
 PGYSGPNCYLTHTLKTLKERFDSEEIKPDLWMSLEGGSTCTECGILAEDTALYFGGST  
 VRQAVTQDLDLRGAKFLQYWGRIGSENNMTSCHRPICRKEGVLLDYSTDGGITWTL LH  
 EMDYQKYISVRHDYILLPEDALTNTTRLRWWQPFVISNGIVVSGVERAQWALDNILIGGA  
 EINPSQLVDTFDDEGTSHEENWSFY PNAVRTAGFCGNPSFHLWPNKKKDKTHNALSS  
 RELIIQPGYMMQFKIVVGCEATSCGDLHSVMLEYTKDARS DSWQLVQTQCLPSSSNSIG

CSPFQFHEATIYNSVNSSSWKRITQLPDHVSSSATQFRWIKGEETEKQSWAIDHVIYIG  
 EACPKLCSGHGYCTTGAICICDESFQGDDCSVFSHDLPSYIKDNFESARVTEANWETIQ  
 GGVIGSGCGQLAPYAHGDSLYFNGCQIRQAATKPLDLTRASKIMFVLQIGSMSQTDSCN  
 SDLSGPHAVDKAVLLQYSVNNGITWHVIAQHQPDKDFTQAQRVSYNVPLEARMKGVLLR  
 WWQPRHNGTGHDQWALDHVEVVLVSTRKQNYMMNFSRQHGLRHFYNRRRRSLRRY  
 P

SEQID No:86

MAEDADMRNELEEMQRRADQLADESLESTRMLQLVEESKDAGIRTLVMLDEQGEQL  
 ERIEEGMDQINKDMKEAEKNLTDLGKFCGLCVCPCNKLKSSDAYKKAWGNNQDGVVA  
 SQPARVVDEREQMAISGGFIRRVTDARENEMDENLEQVSGIIGNLRHMALDMGNEIDT  
 QNRQIDRIMEKADSNKTRIDEANQRATKMLGSG

SEQID No:87

MASTISAYKEKMKELSVLSLICSCFYTQPHPNTVYQYGDMEVKQLDKRASGQSFEVILK  
 SPSDLSPESPMLSSPPKKKDTSLLEELQKRLEAAEERRKTQEAQVLKQLAERREHEREV  
 LHKALEENNNFSRQAEEKLNYKMELSKEIREAHLAALRERLREKELHAAEVRNKEQRE  
 EMSG

SEQID No:88

MKDRTQELRTAKDSDDDDDDVAVTVDRDRFMDEFFEQVEEIRGFIDKIAENVEEVKRKHS  
 AILASPNPDEKTKEELEELMSDIKKTANKVRSKLSIEQSIEQEEGLNRSSADLRIRKTQH  
 STLSRK FVEVMSEYNATQSDYRERCKGRIQRQLEITGRTTTSEELEDMLESGNPAIFAS  
 GIIMDSSISKQALSEIETRHSEIIKLENSIRELHDMFMDMAMLVESQGEMIDRIEYNVEHAV  
 DYVERAVSDTKKAVKYQSKARRKKIMIIICCVILGIVIASTVGGIFA

SEQID No:89

MAASMFYGRLVAVATLRNHRPRTAQRAAAQVLGSSGLFNNHGLQVQQQQQRNLSLHE  
 YMSMELLQEAGVSVPKGYVAKSPDEAYAIKKLGSKDVVIKAQVLAGGRGKGT FESGL  
 KGGVKIVFSPPEAKAVSSQMIGKKLFTKQTGEKGRICNQVLVCERKYPRREYYFAITME  
 RSFQGPVLIGSSHGGVNIEDVAAETPEAIIKEPIDIEEGIKKEQALQLAQKMGFPPNIVESA  
 AENMVKLYSLFLKYDATMIEINPMVEDSDGAVLCMDAKINFDSNSAYRQKKIFDLQDWT  
 QEDERDKDAAKANLNYIGLDGNIGCLVNGAGLAMATMDIIKLHGGTPANFLDVGGGATV

HQVTEAFKLITSDKKVLAILVNIFGGIMRCDVIAQGIVMAVKDLEIKIPVVVRLQGTRVDDA  
KALIADSGLKILACDDLDEAARMVVKLSEIVTLAKQAHVDVKFQLPI

SEQID No:90

MAPLDLDKYVEIARLCKYLPENDLKRLCDYVCDLLEESNVQPVSTPVTVCEDIHQGFY  
DLCELFRTGGQVPDTNYIFMGDFVDRGYYSLETFTYLLALKAKWPDRITLLRGNHESRQ  
ITQVYGFYDECQTKYGNANAWRYCTKVFDMLTVAALIDEQILCVHGGGLSPDIKTLDQIRTI  
ERNQEIPHKGAFCDLVWSDPEDVDTWASPRGAGWLFGAKVTNEFVHINNLLKICRAH  
QLVHEGYKFMFDEKLVTVWSAPNYCYRCGNIASIMVFKDVNTREPKLFRAVPDSERVIP  
PRTTTPYFL

SEQID No:91

MATRSSRRRESRLPFLFTLVALLPPGALCEVWTQRLHGGSAPLPQDRGFLVVQGDPREL  
RLWARGDARGASRADEKPLRRKRSAALQPEPIKVYGGVSLNDSHNQMNVHWAGEKS  
NVIVALARDSLALARPSSDVYVSVDYGKSFKKISDKLNFGGLNRSEAVIAQFYHSPADN  
KRYIFADAYAQYLWITFDFCNTLQGFSSIPFRAADLLLHASKASNLLGLFDRSHPNKQLWKS  
DDFGQTWIMIQEHVKSFSWGIDPYDKPNTIYIERHEPSGYSTVFRSTDFQSSRENQEVL  
EEVRDFQLRDKYMFATKVVHLLGSEQQSSVQLWVSFGRKPMRAAQFVTRHPINEYYIA  
DASEDQVFVVCVSHSNNRTNLYISEAEGLKFSLSLENVLYYSPGGAGSDTLVRYFANEPP  
ADFHRVEGLQGVYIATLINGSMNEENMRSVITFDKGGTWEFLQAPAFTGYGEKINCELS  
QGCSLHLAQRLSQLLNQLRRMPILSKESAPGLIATGSGVGNLASKTNVYISSSAGARW  
REALPGPHYTTWGDHGGIITAIAQGMETNELKYSTNEGETWKTFFSEKPVFVYGLLTP  
GEKSTVFTIFGSNKENVHSLILQVNATDALGVPCTENDYKLWSPSDERGNECLLGHK  
TVFKRRTPHATCFNGEDFDRPVVVSNCSCCTREDYECDFGFKMSDLSLEVCPDPEFS  
GKSYSPVPCPVGSTYRRTRGYRKISGDTCSGGDVEARLEGELVPCPLAEENEFILYAV  
RKSIYRYDLASGATEQLPLTGLRAAVALDFDYEHNCLYWSDALDVIQRLCLNGSTGQE  
VIINSGLTVEALAFEPLSQLLYWVDAGFKKIEVANPDGDFRLTIVNSSVLDRPRALVLP  
QEGVMFWTDWGDLPKGIYRSNMDGSAAYHLVSEDVKWPNGISVDDQWIYWTDAYLE  
CIERITFSGQQRSVILDNLPHPYAIAVFKNEIYWDDWSQLSIFRASKYSGSQMEILANQLT  
GLMDMKIFYKGKNTGSNACVPRPCSLCLPKANNRSRSCRPEDVSSSVLP SGDL MCD  
CPQGYQLKNNTCVKEENTCLRNQYRCSNGNCINSIWWCDFDND CGDMSDERNCPTTI  
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SWVCDGDND CRDWSDEANCTAIYHTCEASN FQCRNGHCIPQRWACDGD TDCQDGS  
DEDPVNCEKKCNGFRCPNGTCIPSSKHCDGLRDCSDGSDEQHCEPLCTHFMDFVCKN

RQQCLFHSMVCDGIIQCRDGSDEDAAFAGCSQDPEFHKVCDEFQFCQNGVCISLIWK  
 CDGMDDCGDYSDEANCENPTEAPNCSRYFQFRCENGHCIPNRWKCDREND CGDWS  
 DEKDCGDSHILPFSTPGPSTCLPNYYRCSSGTCVMDTWVCDGYRDCADGSDEEACPL  
 LANVTAASTPTQLGRCDRFEFECHQPKTCIPNWKRCDCGHQDCQDGRDEANCPHSTL  
 TCMSREFQCEDEGEACIVLSERCDGFLDCSDESDEKACSDELTVYKVQNLQWTADFSG  
 DVTLTWMRPKKMPSASCVYNVYYRVVGESIWKLETHSNKTNTVLKVLKPDTTYQVKV  
 QVQCLSKAHNTNDFVTLRTPEGLPDAPRNLQLSLPREAEGVIVGHWAPPIHGLIREYI  
 VEYSRSGSKMWASQRAASNFT EIKNLLVNTLYTVRVAAVTSRGIGNWSDSKSITTIGK  
 VIPPPDIHIDSYGENYLSFTLTMESDIKVNGYVYNLFWAFDTHKQERRTLNFRGSILSHKV  
 GNLTHTSYEISAWAKTDLGDSPLAFEHVMTRGVRPPAPSLKAKAINQTAVECTWTGP  
 RNVVYGIFYATSFLDLYRNPKSLTTS LHNKTVIVSKDEQYLFLVRVVVPYQGPSSDYVVV  
 KMIPDSRLPPRHLHVHTGKTSVVIKWESPYDSPDQDLLYAIKVDLIRKTD RSYKVKS  
 NSTVEYTLNKLEPGGKYHIIVQLGNMSKDSSIKITTVSLSAPDALKITENDHVLLFWKSLA  
 LKEKHFNESRGYEIHMFD SAMNITAYLGNTTDNFFKISNLKMGHNYTFTVQARCLFGNQI  
 CGEPAILLYDELGSGADASATQAARSTDVAAVVPILFLILLSLGVGFAILYTKHRRQLSS  
 FTAFA NSHYSSRLGSAIFSSGDDLGEDDEDAPMITGFSDDVPMVIA

SEQID No:92

MEGASFGAGRAGAALDPVSFARRPQTLLRVASWVFSIAVFGPIVNEGYVNTDSGPELR  
 CVFNGNAGACRFGVALGLGAFLACAAFLLLDVR FQQISSVRDRRRRAVLLDLGFSGLWS  
 FLWFVGFCFLT NQWQRTAPGPATTQAGDAARAAIAFSFFSILSWVALTVKALQRFRLGT  
 DMSLFATEQLSTGASQAYPGYPVGSGVEGTETYQSPPFTETLDTSPKGYQVPAY

SEQID No:93

MPLRHWGMARGSKPVGDGAQPMAAMGGLKVLLHWAGPGGGEPWVTFSESSLTAE  
 VCIHIAHKVGITPPCFNL FALFDAQAQVWLPPNHILEIPRDASLMLYFRIRFYFRNWHGM  
 NPREPAVYRCGPPGTEASSDQTAQGMQLLDPASFEYLF EQGKHEFVNDVASLWELST  
 EEEIHHFKNESLGM AFLHLCHLALRHGIPLEEVAKKTSFKDCIPRSFRRHIRQHSALT RL  
 LRNVFRRFLRDFQPGRLSQQMVMVKYLATLERLAPRFGTERVPVCHLRLLAQAEGEPC  
 YIRDSGVAPTDPGPESAAGPPTHEVLVTGTGGIQWWPVEEEVNKEEGSSGSSGRNPQ  
 ASLFGKKAKAHKAFGQPADRPREPLWAYFCDFRDITHVVLKEHCVSIHRQDNKCLELSL  
 PSRAAALS FVSLVDGYFRLTADSSHYLCHEVAPPRLVMSIRDGIHGPLEPFVQAKLRPE  
 DGLYLIHWSTSHPYRLILTVAQRSQAPDGMQSLRLRKFP IEQQDGAFVLEGWGRSFPS  
 VRELGAALQGCLLRAGDDCFSLRRCCLPQPGETSNLIIMRGARASPRTLNLSQLSFHRV

DQKEITQLSHLGQGTRTNVYEGRLRVEGSGDPEEGKMDDDEDPLVPGRDRGQELRVVL  
 KVLDPSHHDIALAFYETASLMSQVSHTHLAFVHGVCVRGPENSMVTEYVEHGPLDVWL  
 RRERGHVPMMAWKMVVAQQLASALSYLENKNLVHGNVCGRNILLARLGLAEGTSPFIKL  
 SDPGVGLGALSREERVERIPWLAPECLPGGANSLSAMDKWGFGATLLEICFDGEAPL  
 QSRSPSEKEHFYQRQHRLPEPSCPQLATLTSQCLTYEPTQRPSFRILRDLTRVQPHNL  
 ADVLTVNRDSPAUGPTTFHKRYLKKIRDLGEGHFGKVSLYCYDPTNDGTGEMVAVKAL  
 KADCGPQHRSGWKQEIDILRTLYHEHIIKYKGCCEDQGEKSLQLVMEYVPLGSLRDYLP  
 RHSIGLAQLLLFAQQICEGMAYLHAHDYIHRDLAARNVLLDNDRLVKIGDFGLAKAVPEG  
 HEYYRVREDGDSPVFWYAPECLKEYKFYYASDVWSFGVTLYELLTHCDSSQSPPTKFL  
 ELIGIAQQQMTVLRLTELLERGERLPRPDKCPCEVYHLMKNCWETEASFRPTFENLIPIL  
 KTVHEKYQQQAPS VF SVC

SEQID No:94

MVLIWRRSRYLLREIEAQWSISALWEGFQKWRDNLFLQIVQLIQHVYSVWTASRTVFIKII  
 VTRHTSTGGGFCDGCDTEAWKTGPFCVNHEPGRAGTIKENSRCPLNEEVIVQARKIFP  
 SVIKYVVEMTIWEEEEKELPPELQIREKNERYCYVLFNDEHHSYDHVIYSLQRALDCELA  
 AQLHTTAIDKEGRRRAVKAGAYAACQEAKEDIKSHSENVSQHPLHVEVLHSEIMAHQKFA  
 LRLGSWMNKIMSYSSDFRQIFCQACLREEPDSENPCISRLMLWDALYKYGARKILHELI  
 FSSFFMEMEYKKLFAMEFVKYKQLQKEYISDDHDSISITALSVQMFTVPTLARHLIEE  
 QNVISVITETLLEVLPEYLDNRNNKFNFQGYSDQKLGRVYAVICDLKYILISKPTIWTERLR  
 MQFLEGFRSFLKILTCMQGMEEIRRQVGQHIEVDPDWEAAIAIQMQLKNILLMFQEWCA  
 CDEELLVAYKECHKAVMRCSTSFSSSKTVVQSCGHSLETYSYRVSEDLVSIHLPLSRT  
 LAGLHVRLSRLGAVSRLHEFVSFEDFQVEVLVEYPLRCLVLVAQVVAEMWRRNGLSLIS  
 QVFFYYQDVKCREEMYDKDIIMLQIGASLMDPNKFLLLVLQRYELAEAFNKTISTKDQDLIK  
 QYNTLIEEMLQVLIYVGERYVPGVGNVTKEEVTMREIIHLLCIEPMPHSAIAKNLPEN

SEQID No:95

MKALRLSASALFCLLLINGLGAAPPGRPEAQPPPLSSEHKEPVAGDAVPGPKGDSAPEV  
 RGARNSEPQDEGELFQGVDPRALAAVLLQALDRPASPPAPSGSQQGPEEEAAEALLTE  
 TVRSQTHSLPAAGEPEPAAPPRPQTPENGPEASDPSEELEALASLLQELRDFSPSSAK  
 RQQETAAAETETRTHLTRVNLESPGPERVWRASWGEFQARVPERAPLPPPAPSQFQ  
 ARMPDSGPLPETHKFGGEGVSSPKTHLGEALAPLSKAYQGVAAPFPKARRAESALLGGS  
 EAGERLLQQGLAQVEAGRRQAEATRQAAAEERLADLASDLLLQYLLQGGGARQRLG  
 GRGLQEAAEERESAREEEEEAEQERRGGEERVGEEDEEAAEAAEAEADEAERARQNAL



LFAEEEDGEAGAEDKRSQEETPGHRRKEAEGTEEGGEEEDDEEMDPQTIDSLIELSTK  
 LHLPADDVVSIIEVEEKRNRRKKAPPEVPPPPRAAPATHVRSPQPPPPPPPSARDELP  
 DWNEVLPPWDREEDEVYPPGPYHPFPNYIRPRTLQPPSALRRRHYYHALPPSRHYPG  
 REAQARHAQQEEAEAEERRLQEQEELENYIEHVLLRRP

SEQID No:96

MAHRKLESVGSGMLDHRVRPGPVPHSQEPESEDMELPLEGYVPEGLELAALRPESPA  
 PEEQECHNHSPDGDSSSDYVNNTSEEDYDEGLPEEEEGITYYIRYCPEDDSYLEGMD  
 CNGEEYLAHSAHPVDTDECQEAVEEWTDGAGPHPHGHEAEGSQDYDPGQLPIPEDEP  
 SVLEAHDQEEDGHYCASKEGYQDYYPEEANGNTGASPYRLRRGDGDLEDQEEDIDQI  
 VAEIKMSLSMTSITSASEASPEHGPEPGPEDSVEACPPIKASCSPSRHEARPKSLNLLPE  
 AKHPGDPQGRGFKPKTRTPPEERLKWPHQVCNGLEQPRKQQRSDLNQPVNNDNNIPETK  
 KVASFSPFVAVPGPCEPEDLIDGIIFAANYLGSTQLLSERNPSKNIRMMQAQEA VSRVKR  
 MQKAAKIKKKANSEGDAQTLTEVDLFISTQRIKVLNADTQETMMDHALRTISYIADIGNIV  
 VLMARRRMPPRSASQDCIETTPGAQEGKKQYKMICHVFESEDAQLIAQSIGQA FSVAYQ  
 EFLRANGINPEDLSQKEYSDIINTQEMYNDLIHFSNSENCKELQLEKHKGEILGVVVVE  
 SGWGSILPTVILANMMNGGPAARSGKLSIGDQIMSINGTSLVGLPLATCQGIIKGLKNQT  
 QVKLNIVSCPPVTTVLIKRPDLKYQLGFSVQNGIICSLMRGGIAERGGVRVGHRIIEINGQ  
 SVVATAHEKIVQALSNSVGEIHMKTMPAAMFRLLTGQETPLYI

SEQID No:97

MDTSSVGLELTDQTPVLLGSTAMATSLTNVGNSFSGPANPLVSRSNKFQNSSVEDDD  
 DVVFIQPVQPPPPSVPVADQRTITFTSSKNEELQGNDSKITPSSKELASQKGSVSETIVI  
 DDEEDMETNQGQEKNSSNFIERRPPETKNRTNDVDFSTSSFSRSKVNAGMGNSGITTE  
 PDSEIQIANVTTLETGVSSVNDGQLENTDGRDMNLMITHVTSLQNTNLGDVSNGLQSSN  
 FGVNIQTYTPSLTSQTKTGVPFNPGRMNVAGDVFNQGESATHHNPDSWISQSASFPR  
 NQKQPGVDSLSPVASLPKQIFQPSVQQQPTKPVKVTCANCKKPLQKGQTAYQRKGS  
 HLCSTTCLSSFSHKPAPKKLCVMCKKDITTMKGTIVAQVDSSESFQEFCTSLSLYED  
 KQNPTKGALNKSRTCICGKLTEIRHEVSFKNMTHKLCSDHCFNRYRMANGLIMNCCEQ  
 CGEYLPSKGAGNNVLVIDGQQKRFCQSCVSEYKQVGSHPSFLKEVRDHMQDSFLMQ  
 PEKYGKLTTCTGCRTQCRFFDMTQCIGPNGYMEPYCSTACMNSHKT KYAKS QSLGIIC  
 HFCKRNSLPQYQATMPDGKLYNFCNSSCVAKFQALSMQSSPNGQFVAPSDIQLKCN  
 CKNSFC SKPEILEWENKVHQFC SKTCSDDYKKLHCIVTYCEYCQEEKTLHETVNFSGVK  
 RPFCSSEGCKLLYKQDFARRLGLRCVTCNYCSQLCKKGATKELDGVVVRDFCSEDCKKF

QDWYYKAARCDCKSQGTLKERVQWRGEMKHFCQDQHCLLRFYCQQNEPNMTTQKG  
 PENLHYDQGCQTSRTKMTGSAPPPSPTPNKEMKNKAVLCKPLTMTKATYCKPHMQTK  
 SCQTDDTWRTYVVPVPIPVVYIPVPMHMYSQNIPVPTTVPVVPVPVFLPAPLDSSEKI  
 PAAIEELKSKVSSDALDTELLTMTDMMSEDEGKTETTNINSVIIETDIIGSDLLKNSDPETQ  
 SSMPDVPYEPDLIDFPRAAEELDMENEFLLPPVFGEEYEEQPRPRSKKKGAKRKAV  
 SGYQSHDDSSDNSECSFPFKYTYGVNAWKHWKTRQLDEDLLVLDELKSSKSVKLKE  
 DLLSHTTAELNYGLAHFVNEIRRPNGENYAPDSIYYLCLGIQEYLCGSNRKDNIFIDPGY  
 QTFEQELNKILRSWQPSILPDGSIFSRVEEDYLWRIKQLGSHSPVALLNTLFYFNTKYFG  
 LKTVEQHLRLSFGTVFRHWKKNPLTMENKACLRYQVSSLCGTDNEDKITTKGRKHEDD  
 EPVFEQIENTANPSRCPVKMFECYLSKSPQNLNQRMDVFYLOPECSSSTDSPVWYTST  
 SLDRNTLENMLVRVLLVKDIYDKDNYELDEDTD

SEQID No:98

MARHVFLTGPPGVGKTTLIHKASEVLKSSGVPVDGFYTEEVRQGGRRIGFDVVTLSGTR  
 GPLSRVGLEPPPGKRECRVGQYVVDLTSFEQLALPVLARNADCSSGPGQRVCVIDEIGK  
 MELFSQLFIQAVRQTLSTPGTIILGTIPVPGKPLALVEEIRNRKDVKFVNTKENRNLHLL  
 PDIVTCVQSSRK

SEQID No:99

MAAPPEPGEPEERKSLKLLGFLDVENTPCARHSILYGSLSVAGFGHFLTSRIRRSR  
 DVGVGGFILVTLGCWFHCRYNYAKQRIQERIAREEIKKKILYEGTHLDPERKHNGSSSN

SEQID No:100

MLSLDFLDDVRRMNKRQLYYQVLNFGMIVSSALMIWKGLMVTGSESPIVVVLSGSMEP  
 AFHRGDLLFLTNRVEDPIRVGEIVVFRIEGREIPIVHRVLKIHEKQNGHIKFLTKGDNNAVD  
 DRGLYKQGQHWLEKKDVVGRARGFVPYIGIVTILMNDYPKFYAVLFLLGLFVLVHRE

SEQID

No:101AESDLQLAQIKCNLGRAVQLQELWPGGLFWTRKLSTYIRLYGRKFSKEDHVLFIK  
 LLYELVSIPKLEISM MQGFARLLINLLKKKELLSRADLELPWRPLYDMVERILYSKTEHLG  
 LNWFPSNVENILKTLVKSCRPFYPADATAEMLEEWRLMCPFDVTMQKAITYFEIFLPTS  
 LPPELHHKGFKLWFDELIGLWVSVQNLQPWEGQLVNLFARLATDNIGYIDWDPYVPKIF  
 TRILRSLNLPVGSSQVLVPRFLTNAVDIGHAVIWITAMMGGPSKLQKHLAFLNSITSFY  
 HPSNNGRWLNKLMKLLQRLPNSVVRRLHRERYKKPSWLTPVPDSHKLTDQDVTDFVQ

CIIQPVLLAMFSKTGSLEAAQALQNLALMRPELVIPPVLERTYPALETLTEPHQLTATLSC  
 VIGVARSLVSGGRWFPEGPTHMLPLLMLRALPGVDPNDFSKCMITFQFIATFSTLVPLVD  
 CSSVLQERNDLTEVERELCSATAEFEDFVLQFMDRCFGLIESSTLEQTREETETEKMT  
 LESLVELGLSSTFSTILTQCSKEIFMVALQKVFNSTSHIFETR VAGRMVADMCR AAVKC  
 CPEESLKLFPVPHCCSVITQLTMNDDVLNDEELDKELLWNLQLLSEITRVDGRKLLLYREQ  
 LVKILQRTLHLTCKQGYTLSCNLLHHLLRSTTLIYPTEYCSVPGGFDKPPSEYFPIKDWG  
 KPGDLWNLGIQWHVPSSEEVSAFYLLDSFLQPELVKLQHCGDGKLEMSRDDILQSLTI  
 VHNCLIGSGNLLPPLKGEPVTNLVPSMVSLEETKLYTGLEYDLSRENHREVIATVIRKLLN  
 HILDNSEDDTKSLFLIIKIIGDLLQFQGSHKHEFDSRWKSFNLVKKSMENRLHGKKQHIRA  
 LLIDRVMLQHELRTLTVEGCEYKKIHQDMIRDLLRLSTSSYSQVRNKAQQTFFAALGAYN  
 FCCRDIIPLVLEFLRPDRQGVTTQQQFKGALYCLLGNHSGVCLANLHDWDCIVQTPAIV  
 SSGLSQAMSLEKPSIVRLFDDLAEKIHRQYETIGLDFTIPKSCVEIAELLQQSKNPSINQIL  
 LSPEKIKEGIKRQQEKNADALRNYENLVDTLLDGVEQRNLPWKFEHIGIGLLSLLLRDDR  
 VLPLRAIRFFVENLNHDAIVVRKMAISAVAGILKQLKRTHKKLTINPCEISGCPKPTQIIAGD  
 RPDNHWLHYDSKTIPRTKKEWESSCFVEKTHWGYTWPKNMVVYAGVEEQPKLGRS  
 REDMTEAEQIIFDHFSDPKFVEQLITFLSLEDKRGKDKFNPRRFCLFKGIFRNFDDAFLPV  
 LKPHLEHLVADSHESTQRCVAEIIAGLIRGSKHWTFEKVEKLWELLCPLLRTALSNTIVET  
 YNDWGACIATSCESRDPRKLHWLFELLLESPLSGEGGSFVDACRLYVLQGGGLAQGEW  
 RPELLHRLKYLEPKLTQVYKNVRERIGSVLTYIFMIDVSLPNTTPTISP HVPEFTARILE  
 KKKPLMDVDEEIQNHVMEENGIGEEDEERTQGIIKLLKTLKWL MASAGRSFSTAVTEQLQL  
 LPLFFKIAPVENDNSYDELKRDAKLCLSLMSQGLLYPHQVPLVLQVLKQTARSSSWHAR  
 YTVLTYLQTMVFYNLFIFLNNEDAVKDIRWLVISLLEDEQLEVREMAATTLSGLLQCNFLT  
 MDSPMQIHFEQLCKTKLPKKRKRDPGSGVDTIPSAELVKRHAGVLGLGACVLSSPYDV  
 PTWMPQLLMNLSAHLNDPQPIEMTVKKTLSNFRRTHHDNWQEHKQQFTDDQLLVLTDL  
 LVSPCYA

SEQID No:102

MSDSVILRSIKKFGEENDGFESDKSYNNDDKKSRLQDEKKGDGVRVGGFFQLFRFSSSTDI  
 WLMFVGSLCAFLHGIAQPGVLLIFGTMTDV FIDYDVELQELQIPGKACVNNTIVWTNSSL  
 NQNMTNGTRCGLLNIESEMIKFASYAGIAVAVLITGYIQICFWVIAAARQIQKMRKFYFR  
 RIMRMEIGWFDCNSVGELNTRFSDDINKINDAIADQMALFIQRMTSTICGFLGFFRGWK  
 LTLVIISVSPLIGIGAATIGLSVSKFTDYELKAYAKAGVVADEVISSMRTVAAFGGKEKREVE  
 RYEKNLVFAQRWGIRKGIVMGFFTGFVWCLIFLCYAVAFWYGSTLVLDEGEYTPGTLVQ  
 IFLSVIVGALNLGNASPCLEAFATGRAAATSIFETIDRKPIIDCMSEDGYKLDRIKGEIEFHN

VTFHYPSRPEVKILNDLNMVIKPGEMTALVGPSGAGKSTALQLIQRFYDPCEGMVTVDG  
 HDIRSLNIQWLRDQIGIVEQEPVLFSTTIAENIRYGRE DATMEDIVQAAKEANAYNFIMDL  
 PQQFDTLVGEGGGQMSGGQKQRVAIARALIRNPKILLDMATSALDNESEAMVQEVLS  
 KIQHGHTIISVAHRLSTVRAADTIIGFEHGTAVERGTHEELLERKGVYFTLVTLQSQGNQA  
 LNEEDIKDATEDDMLARTFSRGSYQDSL RASIRQRSKSQLSYLVHEPPLAVVDHKSTYE  
 EDRKDKDIPVQEEVEPAPVRRILKFSAPWPYMLVGSVGA AVNGTVTPLYAFLFSQILG  
 TFSIPDKEEQRSQINGVCLLFVAMGCVSLFTQFLQGYAFAKSGELLTKRLRKFGFRAML  
 GQDIAWFDDL RNSPGALTTRLATDASQVQGAAGSQIGMIVNSFTNVTVMIIAFSFSWK  
 LSLVILCFFPFLALSGATQTRMLTG FASRDKQALEMVGQITNEALSNI RTVAGIGKERRFI  
 EALETELEKPFKTAIQKANIYGFCFAFAQCIMFIANSASYRYGGYLISNEGLHFSYVFRVIS  
 AVVLSATALGRAFSYTPSYAKAKISAARFFQLLDRQPPISVYNTAGEKWDNFQ GKIDFVD  
 CKFTYPSRPDSQVLNGLSVSISPGQTLAFVGSSGCGKSTS IQLLERFYDPDQGKVMIDG  
 HDSKKVNVQFLRSNIGIVSQEPVLFACSIMDNIKYGDNTKEIPMERVIAAAKQAQLHDFV  
 MSLPEKYETNVGSQGSQLSRGEKQRIAIARAIVRDPKILLDEATSALDTESEKTVQVAL  
 DKAREGRTCIVIAHRLSTIQNADIIVMAQG VVIEKGTHEELMAQKGAYYKLVTTGSPIS

SEQID No:103

MSLVLNDLLICCRQLEHDRATERKKEVEKF KRLIRDPETIKHLDRHSDSKQGKYL NWD A  
 VFRFLQKYIQKETEC LRIAKPNVSASTQASRQKKMQEISSLVKYFIKCANRRAPRLKCQE  
 LLNYIMDTVKDSSNGAIYGADCSNILLKDILSVRKYWCEISQQQWLELFSVYFRLYLKPS  
 QDVHRVLVARIIHAVTKGCCSQTDGLNSKFLDFFSKAIQCARQEKSSSGLNHILAALTIFL  
 KTLAVNFRIRVCELGDEILPTLLYIWTQHRLNDSLKEVIIELFQLQIYIHHPKGAKTQEKGA  
 YESTKWR SILYNLYDLLVNEISHIGSRGKYSSGFRNIAVKENLIELMADICHQVF NEDTRS  
 LEISQSYTTTQRESSDYSVPCKRKKIELGWEVIKDHLQKSQNDFDLVPWLQIATQLISKY  
 PASLPNCELSPLLMILS QLLPQQRHGERTPYVLRCLTEVALCQDKRSNLESSQKSDLLK  
 LWNKIWCITFRGISSEQIQAE NFGLLGAIQGS LVEVDREFWKLF TGSACRPSCPAVCCL  
 TLALTTSIVPGAVKMGIEQNMCEVNRSFSLKESIMKWLLFYQLEGDLENSTEVPPI LHSN  
 FPHLVLEKILVSLTMKNCKAAMNFFQSVPECEHHQKDKEELSFSEVEELFLQTTFDKMD  
 FLTIVRECGIEKHQSSIGFSVHQNLKESLDRCLLGLSEQLLNYSSEITNSETLVRC SRLL  
 VGVLG CYCYMGVIAEEEEAYKSELFQKANS LMQCAGESITLFKNKTNEEFRI GSLRNMMQ  
 LCTRCLSNCTKKSPNKIASGFFLRLLTSKLMNDIADICKSLASFIKKPFD RGEVESMEDDT  
 NGNLMEVEDQSSMNLFN DYPDSSVSDANEPGESQSTIGAINPLAEEYLSKQDLLFLDML  
 KFLCLCVTTAQTNTVSFRAADIRRKLLMLIDSSTLEPTKSLHLHMYLM LKELPGEEYPLP  
 MEDVLELLKPLSNVCSLYRRDQDVCKTILNHVLHV VKNLGQSNMDSENTRDAQQQFLT

VIGAFWHLTKERKYIFSVRMALVNCLKTLLEADPYSKWAILNVMGKDFPVNEVFTQFLAD  
NHHQVRMLAAESINRLFQDTKGDSSRLLKALPLKLQQTAFENAYLKAQEGMREMSHA  
ENPETLDEIYNRKSVLLTLIAVVLSCSPICEKQALFALCKSVKENGLEPHLVKKVLEKVSE  
TFGYRRLEDFMASHLDYLVLEWLNLDTEYNLSSFPFILLNYTNIEDFYRSCYKVLIPHLV  
IRSHFDEVKSIANQIQEDWKSLLTDCFPKILVNILPYFAYEGTRDSGMAQQRETATKVYD  
MLKSENLLGKQIDHLFISNLPEIVVELLMTLHEPANSSASQSTDLCDFSGDLDPA NP PP  
FPSHVIKATFAYISNCHKTKLKSILEILSKSPDSYQKILLAICEQAAETNNVYKKHRILKIYHL  
FVSLLLKDIKSGLGGAFAVLRDVIYTLIHYNQRPSCIMDVSLRSFSLCCDLLSQVCQTA  
VTYCKDALENHLHVIVGTLIPLVYEQVEVQKQVLDLLKYLVIDNKNENLYITIKLLDPFPD  
HVVFCDLRITQQKIKYSRGPFSLLEEINHFLSVSVYDALPLTRLEGLKDLRRQLELHKDQ  
MVDIMRASQDNPQDGIMVKLVNLLQLSKMAINHTGEKEVLEAVGSCLGEVGPIDFSTIA  
IQHSKDASYTKALKLFEDKELQWTFIMLTYNNTLVEDCVKVRSAAVTCLKNILATKTGH  
SFWEIYKMTTDPMLAYLQPFRTSRKKFLEVPRFDKENPFEGLDLDINLWIPLSENHDIWIK  
TLTCAFLDSGGTKCEILQLLKPMCEVKTDFCQTVLPYLIHDILLQDTNESWRNLLSTHVQ  
GFFTSCLRHFSQTSRSTTPANLDSESEHFFRCCLDKKSQRTMLAVVDYMRQRKPSS  
GTIFNDAFWLDLNYLEVAKVAQSCAAHFTALLYAEIYADKKSMDDQEKRSALAFEEGSQS  
TTISSLSEKSKEETGISLQDLLLEIYRSIGEPDSLYGCGGGKMLQPITRLRTEHEAMWG  
KALVTYDLETAIPSSSTRQAGIIQALQNLGLCHILSVYLKGLDYENKDWCP ELEELHYQAA  
WRNMQWDHCTSVSKEVEGTSYHESLYNALQSLRDREFSTFYESLKYARVKEVEEMCK  
RSLESVYSLYPTLSRLQAIGELESIGELFSRSVTHRQLSEVYIKWQKHSQLLKDSDFSQ  
EPIMALRTVILEILMEKEMDNSQRECICKDILTKHLVELSILARTFKNTQLPERAIFQIKQYNS  
VSCGVSEWQLEEAQVFWAKKEQSLALSILKQMIKKLDASCAANNPSLKLTYTECLRVCG  
NWLAE TCLENPAVIMQTYLEKAVEVAGNYDGESSDELNRNGKMKAFSLARFSDTQYQR  
IENYMKSSSEFENKQALLKRAKEEVGLLREHKIQTNRYTVKVQRELELDELALRALKEDRK  
RFLCKAVENYINCLLSGEEHDMWVFRCLSLWLENSGVSEVNGMMKRDGMKIPTYKFLP  
LMYQLAARMGTKMMGGLGFHEVLNNLISRISMDHPHHTLFILALANANRDEFLTKEVA  
RRSRITKNVPKQSSQLDEDRTEAANRIICTIRSRRPQMVR SVEALCDAYIILANLDATQW  
KTQRKGINIPADQPITKLKNLEDVVVPTMEIKVDHTGEYGNLVTIQSFKA EFRLAGGVNLP  
KIIDCVGSDGKERRQLVKGRDDL RQDAVMQQVFQMCNTLLQRNTETRKRKLTICTYKV  
VPLSQRSGLVLEWCTGTVPIGEFLVNNE DGAHKRYRPND FSAFQCQKKMMEVQKKSFE  
EKYEVMFMDVCQNFQPVFRYFCMEKFLDPAIWFEKRLAYTRSVATSSIVGYILGLGDRHV  
QNILINEQSAELVHIDLGVAFEQGKILPTPETVPFRLTRDIVDGMGITGVEGVFRRCCEKT  
MEVMRNSQETLLTIVEVLLYDPLFDWTMNPLKALYLQQRPEDETELHPTLNADDQECK

RNLSQIDQSFDKVAERVLMLRQEKLKGVEEGTVLSVGGQVNLLIQQAIDPKNLSRLFPG  
WKAWV

SEQID No:104

MDLEGDRNGGAKKKNFFKLNNKSEKDKKEKKPTVSVFSMFRYSNWLDKLYMVVGTLA  
AIIHGAGLPLMMLVFGEMTDIFANAGNLEDLMSNITNRSNDINDTGFFMNLEEDMTRYAYY  
YSGIGAGVLVAAYIQVSFWCLAAGRQIHKIRKQFFHAIMRQEIGWFDVHDVDELNTRLTD  
DVSKINEGIGDKIGMFFQSMATFFTGFIVGFTRGWKLTVLILAISPVGLLSAAVWAKILSSF  
TDKELLAYAKAGAVAEVLAAIRTVIAFGGQKKELEERYNKNLEEAKRIGIKKAITANISIGA  
AFLLIYASYALAFWYGTTLVLSGEYSIGQVLTVFFSVLIGAFSVGQASPSIEAFANARGAA  
YEIFKIIDNKPSIDSYSKSGHKPDNIKGNLEFRNVHFSYPSRKEVKILKGLNLKVQSGQTV  
ALVGNSGCGKSTTVQLMQRLYDPTGEMVSVSDGQDIRTINVRLREIIGVVSQEPVLFAT  
TIAENIRYGRENVMTDEIEKAVKEANAYDFIMKLPHKFDTLVGERGAQLSGGQKQRIAlA  
RALVRNPKILLLDEATSALDTESEAVVQVALDKARKGRTTIVIAHRLSTVRNADVIAGFDD  
GVIVEKGNHDELMKEKGIYFKLVTMQTAGNEVELENAADESKSEIDALEMSSNDSRSSLI  
RKRSTRRSVRGSQAQDRKLSTKEALDESIPPVSFWRIMKLNLTWPYFVVGVFCAIING  
GLQPAFAIIFSKIIGVFTRIDDPETKRQNSNLFSLFLALGIISFITFFLQGFTFGKAGEILTK  
RLRYMVFRSMLRQDVSWFDDPKNTTGALTTRLANDAAQVKGAIGSRLAVITQNIANLGT  
GIIISFIYGWQLTLLLLAIVPIIAIAGVVEMKMLSGQALKDKKELEGAGKIAIEIENFRTVVS  
LTQEQKFEHMYAQS LQVPYRNSLRKAHIFGITFSFTQAMMYFSYAGCFRFGAYLVAHKL  
MSFEDVLLVFSVAVFGAMAVGQVSSFAPDYAKAKISAAHIIMIIEKTPLIDSYSTEGLMPN  
TLEGNVTFGEVVFNYPTRPDIPVLQGLSLEVKKGQTLALVGSSGCGKSTTVQLLERFYD  
PLAGKVLLDGKEIKRLNVQWLRAHLGIVSQEPILFDCSIAENIAYGDNSRVVSQEEIVRAA  
KEANIHAIESLPNKYSTKVGDKGTQLSGGQKQRIAlARALVRQPHILLLDEATSALDTESE  
EKKVQEALDKAREGRTCIVIAHRLSTIQNADLIVVFQNGRVKEHGTHQQLLAQKGIYFSM  
VSVQAGTKRQ

SEQID No:105

MFSLSSTVQPQFTVPLSHLINAFTPKNTSVSLSGVSVSQNQHRDVVPEHEAPSSECM  
FSDFLTCLNIVSIGKGKIFEGYRSMFMETPAKRMKKS LDTT DNWHIRPEPFSLSIPPSLNLRL  
DLGLSELKIGQIDQLVENLLPGFCKGKNISSHWHTSHVSAQSFFENKYGNLDIFSTLRSS  
CLYRHHSRALQSICSDLQYWPVFIQSRGFKTLKSRTTRRLQSTSERLAETQNIAPSFVKG  
FLLRDRGSDVESLDKLMKTKNIPEAHQDAFKTGFAEGFLKAQALTQKTNDSLRRLILF  
VLLLFGIYGLLKNPFLSVRFRTTTGLDSAVDPVQMKNVTFEHVKGVVEEAKQELQEVVEF

LKNPQKFTILGGKLPKGILLVGPPGTGKTLLARAVAGEADVPFYYASGSEFDEMFGVGVG  
 ASRI RNLFREAKANAPCVIFIDELDSVGGKRIESPMHPYSRQTINQLLAEMDGFKNEGV  
 IIGATNFPEALDNALIRPGRFDMQVTVPRPDVKGRTEILKWYLNKIKFDQSVDPEIARGT  
 VGFSGAELNVLNQAALKA AVDGKEMVTMKELEFSKDKILMGPERRSVEIDNKNKTITA  
 YHESGHAI IAYYTKDAMPINKATIMPRGPTLGHVSLLPENDRWNETRAQLLAQMDVSMG  
 GRVAEELIFGTDHITTGASSDFDNATKIAKRMVTKFGMSEKLGVM TYSDTGKLSPETQS  
 AIEQEIRILLRDSYERAKHILKTHAKEHKNLAEALLTYETLDAKEIQIVLEGKKLEVR

SEQID No:106

MDPSMGVNSVTISVEGMTCN SCVWTIEQQIGKVNGVHHIKVSLEEK NATI IYDPKLQTPK  
 TLQEAIDDMGFD AVIHNP DPLPVLTD TFLTVTASLTLPWDHIQSTLLKTKGVTDIKIYPQK  
 RTVAVTIIPSIVNANQIKELVPELSLDTGTLEKKSGACEDH SMAQAGEVVLKMKVEGMTC  
 HSCTSTIEGKIGKLQGVQRIKVSLDNQEATIVYQPH LISVEEMKKQIEAMGFPAFVKKQP  
 KYLKLGAIDVERLKNTPVKSSEGSQQRSPSYTNDSTATFIIDGMHCKSCVSN IESTLSAL  
 QYVSSIVVSLENRSAIVKYNASSVTPESLRKAIEAVSPGLYRV SITSEVESTSN SPSSSSL  
 QKIPLNVVSQPLTQETVINIDGMTCN SCVQSIEGVISKKPGVK SIRVSLANSNGTVEYDPL  
 LTSPETLRGAIEDMGFDATLSDTNEPLV VIAQPSSEMPLLTSTNEFYTKGMTPVQDKEE  
 GKNSSKCYIQVTGMTCASC VANIERNL RREEGIYSILVALMAGKAEVRYNPAVIQPPMIA  
 EFIRELGF GATVIENADEGDGVLELVVRGMTCASC VHKIESSLTKHRGILYCSVALATNK  
 AHIKYDPEIIGPRDIHTIESLGFEASLVKKDRSASHLDHKREIRQWRRSFLVSLFFCIPVM  
 GLMTYMMVMMDH HFATLHHNQNM SKEEMINLHSSMFLERQILPGLSVMNLLSFLLCVPV  
 QFFGGWYFYIQAYKALKHKTANMDVLIVLATTIAFAYSLIILLVAMYERAKVNPITFFDTPP  
 MLFVFIALGRWLEHIAKGKTSEALAKLISLQATEATIVTLDSDNILLSEEQVDVELVQRGDII  
 KVVPGGKFPVDGRVIEGHSMVDESLITGEAMPVAKKPGSTVIAGSINQNGSLLICATHVG  
 ADTTLSQIVKLVEEAQTSKAPIQQFADKLSGYFVPFIVFSIATLLVWIVIGFLNFEIVETYF  
 PGYNRSISRTETIIRFAFQASITVLCIACPCSLGLATPTAVMVG TGVGQAQNGILIKGGEPL  
 MAHKVKVVVFDKTGTITHGTPVVNQVKVLTESNRISHHKILAIVGTAESNSEHPLGTAITK  
 YCKQELDTETLGT CIDFQVVP GCGISCKVTNIEGLLHKNNWNIEDN NIKNASLVQIDASN  
 EQSSTSSSMIIDAQISNALNAQQHKVLIGNREWMIRNGLVINNDVND FMT EHERKGRTA  
 VLVAVDDEL CGLIAIADTVKPEAE LAIHILKSMGLEVV LMTGDNSKTARSIASQVGITKVFA  
 EVLP SHKVAKVKQLQEEGKRVAMVGDGINDSPALAMANVGIAIGTGT DVAIEAADVVLIR  
 NDLLDVVASIDLSRKT VKRIRINFV FALIYNLVGIPIAAGVFMPIGLVLPWMGSAAMAAS  
 SVSVVLSLFLKLYRKPTYESYELPARSQIGQKSPSEISVHVGIDDTSRNSPKLGLLDRIV  
 NYSRASINSLLSDKRSLSNVVTSEPDKHSLLVGDFREDDDTAL

SEQID No:107

METPAAAAPAGSLFPSFLLACGTLVAALLGAAHRLGLFYQLLHKVDKASVRHGGENVA  
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 VTAGPGLTNTVTAVKNAQMAQSPILLGGAASTLLQNRGALQAVDQLSLFRPLCKFCVS  
 VRRVRDIVPTLRAAMAAQSGTPGPVFVELPVDVLYPYFMVQKEMVPAKPPKGLVGRV  
 VSWYLENYLANLFAGAWEPQPEGPLPLDIPQASPQQVQRCVEILSRAKRPLMVLGSQA  
 LLTPTSADKLRAAVETLGVPCFLGGMARGLLGRNHPLHIRENRSAAKKADVIVLAGTVC.  
 DFRLSYGRVLSHSSKIIIVNRNREEMLLNSDIFWKPQEAVQGDVGSFVLKLVEGLQGQT  
 WAPDWVEELREADRQKEQTFREKAAMPVAQHLNPVQVLQLEETLPDNSILVVDGGD  
 FVGTAHLVQPRGPLRWLDPGAFGTLGVGAGFALGAKLCPDAEVWCLFGDGAFGYS  
 LIEFDTFVRHKIPVMALVGNDAGWTQISREQVPSLGSNVACGLAYTDYHKAAMGLGAR  
 GLLLSRENEDQVVKVLHDAQQCCRDGHPVVVNILIGRTDFRDGSIIV

SEQID No:108

MPVLSRPRPWGNTLKRRTAVLLALAAYGAHKVYPLVRQCLAPARGLQAPAGEPTQEAS  
 GVAAAKAGMNRVFLQRLLWLLRLLFPRVLCRETGLLALHSAALVSRTFLSVYVARLDGR  
 LARCIARKDPRAFGWQLLQWLLIALPATFVNSAIRYLEGQLALSFRSRLVAHAYRLYFSQ  
 QTYRVSNDMDGRLRNPQSLTEDVVAFAASVAHLYSNLTKPLLDVAVTSYTLLRAARSR  
 GAGTAWPSAIALGLVVFLTANVLRAFSPKFGELVAEEARRKGELRYMHSRVVANSEEIAF  
 YGGHEVELALLQRSYQDLASQINLILLERLWYVMLEQFLMKYVWSASGLLMVAVPIITAT  
 GYSESDAEAVKKALEKKEEELVSETEAFTIARNLLTAAADAIERIMSSYKEVTELAGYT  
 ARVHEMFQVFEDVQRCHFKRPRELEDAQAGSGTIGRSGVRVEGPLKIRGQVVDVEQGI  
 ICENIPIVTPSGEVVVASLNIRVEEGMHLLITGPNCGCKSSLFRILGGLWPTYGGVLYKPP  
 PQRMFYIPQRPYMSVGSRLDQVIYPDSVEDMQRKGYSEQDLEAILDVVHLHHILQREG  
 GWEAMCDWKDVLSGGEKQRIGMARMFYHRPKYALLDECTSAVSIDVEGKIFQAAKDA  
 GIALLSITHRPSLWKYHTHLLQFDGEGGWKFELDSAARLSLTEEKQRLEQQLAGIPKM  
 QRRQLQELCQILGEAVAPAHVPAPSPQGPGLQAST

SEQID No:109

MGAAVFFGCTFVAFGPAFALFLITVAGDPLRVIIIVAGAFFWLVSLLASVWVILVHVTD  
 RSDARLQYGLLIFGAAVSVLLQEVFRFAYYKLLKKADEGLASLSEDGRSPISIRQMAYVS  
 GLSFGIISGVFSVINILADALGPGVVGIIHGDSPIYFLTSAFLTAAILLHTFWGVVFFDACE



RRRYWALGLVVGSHLLTSGLTFLNPWYEASLLPIYAVTVSMGLWAFITAGGSLRSIQRS  
LLCRRQEDSRVMVYSALRIPPED

SEQID No:110

MYEGKKTKNMFLTRALEKILADKEVKKAHHSQLRKACEVALEEIKAETEKQSPPHGEAK  
AGSSTLPPVKSKTNFIEADKYFLPFELACQSKCPRIVSTSLDCLQKLIAYGHILTGNAPDST  
TPGKKLIDRIIETICGCFQGPQTDEGVQLQIIKALLTAVTSQHIEIHEGTVLQAVRTCYNIL  
ASKNLINQTTAKATLTQMLNVIFARMENQALQEAKQMEKERHRQHHLPLSPVSHHEP  
ESPQLRYLPPQTVDHISQEHEGDLHTNDVDKSLQDDTEPENGS DISSAENEQTEAD  
QATAAETLSKNEVLYDGENHDCEEKPQDIVQNIVEEMVNIVVGDMGEGTTINASADGNI  
GTIEDGSDSENIQANGIPGTPISVAYTPSLPDDRSLVSSNDTQESGNSSGSPSPGAKFSHI  
LQKDAFLVFRSLCKLSMKPLSDGPPDPKSHELRSKILSLQLLLSILQNAGPIFRTNEMFIN  
AIKQYLCVALSKNGVSSVPEVFELSLSIFLTLLSNFKTHLKMQUIEVFFKEIFLYILETSTSSF  
DHKWMVIQTLTRICADAQSVVDIYVNYDCDLNAANIFERLVNDLSKIAQGRGSQELGMS  
NVQELSLRKKGLECLVSISKCMVEWSKDQYVNPNSQTTLGQEKPEQEMSEIKHPETIN  
RYGSLNSLESTSSSGIGSYSTQMSGTDNPEQFEVLKQQKEIIEQGIDLFNKKPKRGIQYL  
QEQQMLGTTPEIDIAQFLHQEERLDSTQVGEFLGDNDKFNKEVMYAYVDQHDFSGKDF  
VSALRMFLEGFRLPGEAQKIDRLMEKFAARYLECNQGQTLFASADTAYVLAYSIIMLTTD  
LHSPQVKNKMTKEQYIKMNRGINDSKDLPEEYLSAIYNEIAGKKISMKETKELTIPTKSSK  
QNVASEKQRRLLYNLEMEQMAKTAKALMEAVSHVQAPFTSATHLEHVRPMPFKLAWTP  
FLAAFSVGLQDCDDTEVASLCLEGIRCAIRIACIFSILQERDAYVQALARFTLLTVSSGITE  
MKQKNIDTIKTLITVAHTDGNYLGNWHEILKCISQLKLAQLIGTGVPKYISGTVRGREG  
SLTGTKDQAPDEFVGLGLVGGNVWDWKQIASIQESIGETSSQSVVAVDRIFTGSTRLDG  
NAIVDFVRWLCVSMDELLSTTHPRMFSLQKIVEISYYNMGRIRLQWSRIWEVIGDHFNK  
VGCNPNEDVAIFAVDSLRLQLSMKFLEKGELANFRFQKDFLRPFHIMKRNRSPTIRDMV  
VRCIAQMVNSQAANIRSGWKNIFS VFH LAASDQDESIVELAFQTTGHIVTLVFEKHFPATI  
DSFQDAVKCLSEFACNAAFPDTSM EAIRLIRHCAKYVSDRPQAFKEYTSDDMNVPED  
RVWVRGWFPILFELSCIINRCKLDVRTRGLTVMFEIMKTYGHTYEKHHWWQDLFRIVFRIF  
DNMKLPEQQTEKA EWMTTTCNHALYAICDVFTQYLEVLSDVLLDDIFAQLYWCVQQDN  
EQLARSGTNCLENVVILNGEKFTLEIWDKTCNCTLDIFKTTIPHALLTWRPNSETAPPP  
PSPVSEKPLDTISQKSVDIHDSIQPRSDNRPQAPLV SASAVNEEVSKIKSTAKFPEQKL  
FAALLIKCVVQLELIQTIDNIVFFPATSKKEDAENLAAQ RDAVDVDFVRVDTQDQGM YRF  
LTSQQLFKLLDCLLESHRFAKAFNSNNEQRTALWKAGFKGKSKPNLLKQETSSLACGLR

ILFRMYMDES RVSAWEEVQQRLLNVCSEALSYFLT LTSESHREAWTNLLLLFLTKVLKIS  
DNRFKAHASFYYP LLCEIMQFDLIP ELRAVLRRFFLRIGVVFQISQPPEQELGINKQ

SEQID No:111

MAVSRLDRLFILLDTGTPVTRKAAAQQLGEVVKLHPHELNNLLSKVLIYLR SANWDTRI  
AAGQAVEAIVKNVPEWNPVPRTRQEPTSESSMEDSPTTERLNFD RFDICRLLQH GASLL  
GSAGAEFEVQDEKSGEVDPKERARQRKLLQKKLGLNMGEAIGMSTEELFNDEDLDYT  
PTSASFVNKQPTLQAAELIDSEFRAGMSNRQKNKAKRMAKLF AKQRSRDAVETNEKSN  
DSTDGEPEEKRRKIANVVINQSANDSKVLIDNIPDSSSLIEETNEWPLESFCEELCNDLFN  
PSWEVRHGAGTGLREILKAHGKSGGKMGDSTLEEMIQQH QEWLEDLVIRLLCVFALDR  
FGDFVSDEVVAPVRETCAQTLGVVLKHMNETGVHKTVDVLLKLLTQEQWEVRHGGLLG  
IKYALAVRQDVINTLLPKVLTRII EQLQDLDDVRAVAAASLVPVVESLVYLQTQKVPFIIN  
TLWDALLELDDLTASTNSIMTLLSSLLTYPQVQQCSIQQSLTVLVPRVWPFLHHTISSVR  
RAALETFTLLSTQDQNSSSWLIPILPDMLRHIFQFCVLESSQEILD LIHKVWMELLSKAS  
VQYVVAACCPWMGAWLCLMMQPSHLPIDLNMLLEV KARAKEKTGGKVRQGGQSQNKE  
VLQEYIAGADTIMEDPATRDFVVMRARMMAAKLLGALCCCICDPGVNVVTQEIKPAESL  
GQLLLFHLNSKSALQRISVALVICEWAALQKECKAVTLAVQPRLLDILSEHLYYDEIAVPF  
TRMQNECKQLISSLADVHIEVGNRVNNNVLTIDQASDLVTTVFNEATSSFDLNPQVLQQ  
LDSKRQQVQMTVTETNQEWQVLQLRVHTFAACAVVSLQQLPEKLNPIIKPLMETIKKEE  
NTLVQNYAAQCI AKLLQQCTTRTPCPNSKIIKNLCSSLCVDPYLTPCVTCVPVPTQSGQEN  
SKGSTSEKDGMHHTVTKHRGIITLYRHQKA AFAITSRRGPTPKAVKAQIADLPAGSSGNI  
LVELDEAQKPYLVQRRGA EFALTTIVKHFGGEMAVKLPHLWDAMVGPLRNTIDINNFDG  
KSLLDKGDSPAQELVNSLQVFETA AASMDSELHPLL VQHLP HLYMCLQYPSTAVRHMA  
ARCVGVMSKIATMETMNIFLEKVL PWLGAI DSVKQEGAIEALACVMEQLDVGIVPYIVLL  
VVPVLGRMSDQTD SVRFMATQCFATLIRLMPLEAGIPDP PNMSAELIQLKAKERHFLEQ  
LLDGKKLENYKIPVPINAELRKYQQDGVNWL AFLN KYKLHGILCDDMGLGKTLQ SICILA  
GDHCHRAQEYARSKLAECMPLPSLVVCPPTLTGHWVDEVGKFC SREYLNPLHYTGPP  
TERIRLQH QVKRHNLIVASYDVVRNDIDFFRNIKFNYCILDEGHV IKN GKTKLSKAVKQLT  
ANYRIILSGTPIQNNVLELWSLFD FLMPGFLGTERQFAARYGKPILASRDARSSSREQEA  
GVLAMDALHRQVLPFLLRRMKEDVLQDLPPKIIQDYYCTLSPLQVQLYEDFAKSRAKCD  
VDET VSSATLSEETEKPKLKATGHVFQALQYLRKLCNHPALVLT PQHPEFKTTAEKLAV  
QNSSLHDIQHAPKLSALKQLLLD CGLGNGSTSES GTESVVAQHRILIFCQLKSMLDIVEH  
DLLKPHLPSVTYLRLDGSIPPGQRHSIVSRFNNDPSIDVLLL TTHVGGLGLNLTGADTVV  
FVEHDWNPMRDLQAMDRAHRIGQKR VNVYRLITRG TLEEKIMGLQKF KMNIANTVISQ

ENSSLQSMGTDQLLDLFTLDKDGKAEKADTSTSGKASMKSILENLSDLWDQEQYDSEY  
SLENFMHSLK

SEQID No:112

MGGRVFLAFCVWLTLPGAETQDSRGCARWCPQNSSCVNATAACRCNPGFSSSFSEIITTP  
TETCDDINECATPSKVSCGKFSDCWNTGSDCVCSPGYEPVSGAKTFKNESENTCQ  
DVDECQQNPRLCKSYGTCVNTLGSYTCQCLPGFKFIPEDPKVCTDVNECTSGQNPCH  
SSTHCLNNGVGSYQCRCPGWQPIPGSPNGPNNTVCEDVDECSSGQHQCDSSTVCFN  
TVGSYSCRCRPGWKPRHGIPNNQKDTVCEDMTFSTWTPPPGVHSQTLRFFDKVQDL  
GRDSKTSSAEVTIQNVIKLVDELMEAPGDVEALAPPVRHLIATQLLSNLEDIMRILAKSLP  
KGPFTYISPSNTELTLMIQERGDKNVTMGQSSARMKLNWAVAAGAEDPGPAVAGILSIQ  
NMTTLLANASLNLHKKQAELEEIYESSIRGVQLRRLSAVNSIFLSHNNTKELNSPILFAF  
SHLESSDGEAGRDPAPAKDVMPGPRQELLCAFWKSDSDRGGHWATEVCQVLGSKNGS  
TTCQCSSLSSFTILMAHYDVEDWKLTLITRVGLALSFLCLLLCILTFLVRPIQGSRTTIHL  
HLCICLFVGSTIFLAGIENEGGQVGLRCRLVAGLLHYCFLAAFCWMSLEGLELYFLVVRV  
FQQQGLSTRWLCLIGYGVPLLIVGVSAAIYSKGYGRPRYCWLDFEQGFLWSFLGPVTFII  
LCNAVIFVTTVWKLTKQFSEINPDMKKLKKARALTITAIQFLLGCTWVFGLFIFDDRSLV  
LTYVFTILNCLQGAFLYLLHCLLNKKVREEYRKWACLVAGGSKYSEFTSTTSGTGHNQT  
RALRASESGI

SEQID No:113

SLQWTAVATFLYAEEFVVLCCIPFISPKRWQKIFKSRLVELLVSYGNTFFVVLIVILVLLVI  
DAVREIRKYDDVTEKVNQLQNNPGAMEHFHMKLFRAQRNLYIAGFSLLLSFLRLRLVTLS  
QQATLLASNEAFKKQAESASEAAKKYMEENDQLKKGAAVDGGKLDVGNAEVLKEEEN  
RSLKADLQKLKDELASTKQKLEKAENQVLAMRKQSEGLTKEYDRLLLEEHAQLQAAVDG  
PMDKKEE

SEQID No:114

MSFLIDSSIMITSQILFFGFGWLFFMRQLFKDYEIRQYVVQVIFSVTFASFCTMFELIIFEIL  
GVLNSSSRYFHWKMNLVCVILLILVFMVPFYIGYFIVSNIRLLHKQRLLFSCLLWLTFMYFF  
WKLGDPPFIPILSPKHGILSIEQLISRVGVIGVTLMALLSGFGAVNCPYTYMSYFLRNVTDTD  
ILALERLLQTMDMIISKKKRMAMARRTMFQKGEVHNKPSGFWGMIKSVTTSASGSEN  
TLIQQEVDALAEELSRLFLFETADLYATKERIEYSKTFKGKYFNFLGYFFSIYCVWKIFMATI  
NIVFDRVGKTDVPVTRGIEITVNYLGIQFDVKFWSQHISFILVGIIIVTSIRGLLITLTKFFYAI

SSKSSNVIVLLLAQIMGMYFVSSVLLIRMSMPLEYRTIITEVLGELQFNFYHRWFDVIFLVS  
ALSSILFLYLAHKQAPEKQMAP

SEQID No:115

GEGGESWPPPVRVRGVGVALTCSSATADPPSALSSRRSVPPGQLCEAAAGEGTMG  
TVHARSLEPLPSSGPDFGGLGEEAEFVEVEPEAKQEILENKDVVVQHVHFDGLGRTKD  
DIIICEIGDVFKAKNLIEVMRKSHEAREKLLRLGIFRQVDVLIDTCQGDDALPNGLDVTFEV  
TELRRLTGSYNTMVGNNEGSMVLGLKLPNLLGRAEKVTFQFSYGTKETSYGLSFFKPR  
PGNFERNFSVNLYKVTGQFPWSSLRETDRGMSAEYSFPIWKTSHTVKWEGVWRELGC  
LSRTASFAVRKESGHSLKSSLSHAMVIDSRNSSILPRRGALLKVNQELAGYTGGDVFSIK  
EDFELQLNKQLIFDSVFSASFWGGMLVPIGDKPSSIADRFYLGGPSTIRGFSMHSIGPQS  
EGDYLGGEAYWAGGLHLYTPLPFRPGQGGFGELFRTHFFLNAGNLCNLNYGEGPKAHI  
RKLAECIRWSYGAGIVLRLGNARLELNYCVPMGVQTGDRICDGVQFGAGIRFL

SEQID No:116

MALAVSLPLALSPPRLLLLLLSLLPVARASEAEHRLFEDYNEIIRPVANVSDPVIIHF  
EVSMSQLVKVDEVNQIMETNLWLKQIWNDYKLKWNPSDYGGAEFMRVPAQKIWKPDIV  
LYNNAVGDFFQVDDKTKALLKYTG EVTWIPPAIFKSSCKIDVTYFPFDYQNCTMKFGSWS  
YDKAKIDLVLIGSSMNLKDYWESGEWAIKAPGYKHDIKYNCCEEIYPDITYSLYIRRLPLF  
YTINLIIPCLLISFLTVLV FYLPSDCGEKVTLCSVLLSLTVFLLVITETIPSTSLVIPLIGEYLLF  
TMIFVTLSIVITVFVLNVHYRTPTTHTMPSWVKTVFLNLLPRVMFMTRPTSNEGNAQKPR  
PLYGAELSNLNCFSRAESKGCKEGYPCQDGMCGYCHHRIKISNFSANLTRSSSES  
DAVLSLSALSPEIKEAIQSVKYIAENMKAQNEAKEIQDDWKYVAMVIDRIFLWVFTLVCIL  
GTAGLFLQPLMAREDA

SEQID No:117

MGSRASTLLRDEELEEIKKETGFSSHSQITRLYSRFTSLDKGENGTLSREDFQRIPELAINP  
LGDRIINAFFPEGEDQVNFRGFMRTLAHFRPIEDNEKSKDVNGPEPLNSRSNKLHFAFR  
LYDLDKDEKISRDELLQVLRMMVGVNISDEQLGSIADRTIQEADQDGD SAISFTEFVKVL  
EKVDVEQKMSIRFLH

SEQID No:118

MAESSPLLAYRLLGEEGVALPANGAGGPGGASARKLSTFLGVVPTVLSMFSIVVFLRI  
GFVVGHAGLLQALAMLLVAYFILALTVLSVCAIATNGAVQGGGAYFMISRTLGP EVGGS

GLMFYLANVCGCAVSLLGLVESVLDVFGADATGPSGLRVLPQGYGWNLLYGSLLLGLV  
GGVCTLGAGLYARASFLTLLVSGSLASVLISFVAVGPRDIRLTPRPGPNGSSLPPRFGH  
FTGFNSSTLKDNLGAGYAEDYTTGAVMNFANVFAVLNFGCTGIMAGANMSGELKDPSR  
AIPLGTIVAVAYTFFVYVLLFFLSSFTCDRTLQEDYGFFRAISLWPPLVLIGIYATALSAS  
MSSLIGASRILHALARDDLFGVILAPAKVVSRRGNPWAAVLYSWGLVQLVLLAGKLNLA  
AVTVFYLVAYAAVDLSCLSLEWASAPNFRPTFSLFSWHTCLLGVASCLLMMFLISPGA  
AGGSLLLMGLLAALLTARGGPSSWGYVSQALLFHQVRKYLLRLDVRKDHVKFWRPQLL  
LLVGNPRGALPLRLANQLKKGGLYVLGHVTLGDLDLSPDPVQPQYGAWLSLVDRAQ  
VKAFVDLTFSPSVRQGAQHLLRISGLGGMKPNTLVLGFYDDAPPQDHFLTDPAFSEPAD  
STREGSSPALSTLFPPPRAPGSPRALNPQDYVATVADALKMNKNVVLARASGALPPER  
LSRSGSGGTSQLHHVDVWPLNLLRPRGGPGYVDVCGFLFLQMATILGMVPAWHSARLRI  
FLCLGPREAPGAAEGRLRALLSQLRIRAEVQEVWGEAGAGEPEAEEEGDFVNSGR  
GDAAEALARSANALVRAQQGRGTGGGPGGPEGGDAEGPITALTFLYLPRPPADPAR  
YPRYLALLETLTRDLGPTLLVHGVTPVTCTDL

SEQID No:119

MASFVTEVLAHSGRLEKEDLGTRISRLTRRVEEIKGEVCNMISKKYSEFLPSMQSAQGLI  
TQVDKLSEDIDLLKSRIESEVRRDLHVSTGEFTDLKQQLERDSVLSLLKQLQEFSTAIEE  
YNCALTEKKYVTGAQRLEEAQKCLKLLKSRKCFDLKILKSLSMELTIQKQNILYHLGEEW  
QKLIVWKFPSPSKDTSSLESYLQTELHLYTEQSHKEEKTMPPISSVLLAFSVLGELHSLK  
KSFGQMLLKYLRLPLASCPSLHAVIESQPNIVIRFESIMTNLEYPSPPSEVFTKIRLVLEVLO  
KQLDLPLDLDLENEKTSTVPLAEMLGDMIWEDLSECLIKNCLVYSIPTNSSKLQQYEEII  
QSTEEFENALKEMRFLKGDTTDLLKYARNINSHFANKKQCDVIVAARNLMTSEIHNTVKII  
PDSKINPELPTPDEDNKLEVQKVSNTQYHEVMNLEPENTLDQHSFSLPTCRISESVKK  
LMELAYQTLLEATTSSDQCAVQLFYSVRNIFHLFHDVVPTYHKENLQKLPQLAAIHHNNC  
MYIAHHLLTLGHQFRLRLAPILCDGTATFVDLVPGFRLGTECFQAQMRAQKGELLERLS  
SARNFSNMDEENYSAASKAVRQVLHQLKRLGIVWQDVLPVNIYCKAMGTLLNTAISEV  
IGKITALEDISTEDGDRLYSLCKTVMDEGPQVFAPLSEESKNKKYQEEVPVYVPKWMPF  
KELMMMLQASLQEIGDRWADGKGPLAAAFSSSEVKALIRALFQNTERRAAALAKIK

SEQID No:120

MSRLGALGGARAGLGLLLGTAAGLGFLCLLYSQRWKRTQRHGRSQSLPNSLDYTQTS  
DPGRHVMILLRAVPGGAGDASVLPPLPREGQEKVLDRLDFVLTSLVALRREVEELRSSL  
RGLAGEIVGEVRCHMEENQRRVARRRRFPFVRERSDSTGSSSVYFTASSGATFTDAESE

GGYTTANAESDNERDSKEDGEDEVSCETVKMGRKDSLDEEEAASGASSALEAG  
 GSSGLEDVLP LLQQADELHRGDEQGKREGFQLLLNNKLVYGSRQDFLWRLARAYS DM  
 CELTEEVSEKKSALDGKEEAEEAALEKGDDESADCHLWYAVLCGQLAEHESIQRRIQSGF  
 SFKEHVDKAIALQPENPMAHFLLGRWCYQVSHLSWLEKKTATALLSPLSATVEDALQS  
 FLKAEELQPGFSKAGRVIYISKCYRELGKNSEARWWWMLALELPDVTKEDLAIQKDLEEL  
 EVILRD

SEQID No:121

EIEQNSAMAPRKRGGRGISFIFCCFRNNDHPEITYRLRND SNFALQTM EPALPMP PVEE  
 LDVMFSELVDELDTDKHREAMFALPAEKKWQIYCSKKKDQEENKGATSWPEFYIDQL  
 NSMAARKSLLALEKEEEEEERSKTIESLKTALRTKPMRFVTRFIDL DGLSCILNFLKTMDYE  
 TSESRIHTSLIGCIKALMNNSQGRAHVLAHSESIN VIAQSLSTENIKTKVAVLEILGAVCLV  
 PGGHKKVLQAMLHYQKYASERTRFQTLINDLDKSTGRYRDEVSLKTAIMSFINAVLSQG  
 AGVESLDFRLHLRYEFLMLGIQPVIDKLREHENSTLDRHLDFFEMLRNEDELEFAKRFEL  
 VHIDTKSATQMFELTRKRLTHSEAYPHFMSILHHCLQMPYKRSGNTVQYWLLLDRIIQQI  
 VIQNDKGQDPDSTPLENFNIKNVVRMLVNENEVKQWKEQAEKMRKEHNELOQKLEKK  
 ERECDAKTQEKEEMMQTLNKMKEKLEKETTEHKQVKQQVADLTAQLHEL SRRAVCASI  
 PGGPSPGAPGGPFPSSVPGSLLPPPPPPPLPGGMLPPPPPPPLPPGGPPPPPPGPPPLG  
 AIMPPPGAPMGLALKKKKSIPQPTNALKSFNWSKLPENKLEGTWTEIDDTKVFKILDLED  
 LERTFSAYQRQQDFFVNSNSKQKEADAIDDTLSSKLKVKELSVIDGRR AQNCNILLSRLK  
 LSNDEIKRAILTMDEQEDLPKDMLEQLLK FVPEKSDIDLLEEHKHELD RMAKADRFLFEM  
 SRINHYQQRLQSLYFKKKFAERVAEVKPKVEAIRSGSEEVFRSGALKQLLEVVLAFGN Y  
 MNKGQRGNAYGFKISSLNKIADTKSSIDKNITLLHYLITIVENKYPSVLNLNEELRDIPQAA  
 KVNMTELDKEISTLRSGLKAVETELEYQKSQPPQPGDKFVSVVSQFITVASFSFSDVEDL  
 LAEAKDLFTKAVKHFGEEAGKIQPDEFFGIFDQFLQAVSEAKQENENMRKKKEEEERRA  
 RMEAQLKEQRERERKMRKAKENSEESGEFDDLVSALRSGEVFDKDL SKLKRNRKRITN  
 QMTDSSRERPITKLN F

SEQID No:122

MTVFRQENVDDYYDTGEELGSGQFAVVKKCREKSTGLQYAAKFIKKRRTKSSRRGVSR  
 EDIEREVSILKEIQHPNVITLHEVYENKTDVILILELVAGGELFD FLAEKESLTEEEATEFLK  
 QILNGVYYLHSLQIAHFDLKPENIMLLDRNVKPRIKIIDFGLAHKIDFGNEFKNIFGTPEFV  
 APEIVNYEPLGLEADMWSIGVITYILLSGASPFLGDTKQETLANVSAVN YEFED EYFSNT  
 SALAKDFIRRLLVKDPKKRMTIQDSLQHPWIKPKDTQQALS RKASAVNMEKFKKFAARK

KWKQSVRLISLCQRLSRSFLSRSNMSVARSDDTLDEEDSFVMKAIHAINDDNVPGLQH  
 LLGSLSNYDVNQPNKHGTPPLLIAAGCGNIQILQLLIKRGSRIDVQDKGGSNAVYWAARH  
 GHVDTLKFLSENKCPLDVKDKSGEMALHVAARYGHADVAQVTCAASAPIISRTKEEET  
 PLHCAAWHGYYSVAKALCEAGCNVNIKNREGETPLLTASARGYHDIVECLAHEHGADLN  
 ACDKDGHIHLAVRRCQMEVIKTLLSQGCFVDYQDRHGNTPLHVACKDGNMPIVVAL  
 CEANCNLDISNKYGRTPHLAANNGLDVVRYLCLMGASVEALTTDGKTAEDLARSEQH  
 EHVAGLLARLRKDTHRGLFIQQLRPTQNLQPRIKLLFGHSGSGKTTLVESLKCGLLRSF  
 FRRRRPRLSSTNSSRFPPSPASKPTVSVSINNLYPGCENVSVRSRSMFEPGLTKGM  
 LEVFPVAPTHHPHCSADDQSTKAIDIQNAYLNGVGDFSWEFSGNPVYFCCYDYFAAND  
 PTSIHVVVFSLEEPYEIQLNPVIFWLSFLKSLVPVEEPIAFGGKLNPLQVVLVATHADIMN  
 VPRPAGGEFGYDKDTSLLKEIRNRFGNDLHISNKLFLVDAGASGSKDMKVLNRNHLQEIR  
 SQIVSVCPPMTHLCEKIISTLPSWRKLNGPNQLMSLQQFVYDVQDQLNPLASEEDLRRI  
 AQLHSTGEINIMQSETVQDVLLDPRWLCTNVLGKLLSVETPRALHHYRGRYTVEDIQ  
 RLVPDSDVEELLQILDAMDICARDLSSGTMVDVPALIKTDNLHRSWADEEDEVMVYGGV  
 RIVPVEHLTPFPCGIFHKVQVNLCRWIHHQQSTEGDADIRLWVNGCKLANRGAELLVLLV  
 NHGQGIEVQVRGLETEKIKCCLLLDSVCSTIENVMATTLPGLLTVKHLYSPQQLEHHEP  
 VMIYQPRDFFRAQTLKETSLTNTMGGYKESFSSIMCFGCHDVYSQASLGMDIHASDLNL  
 LTRRKLRLDPPDPLGKDWCLLAMNLGLPDLVAKYNTNNGAPKDFLPSPLHALLREW  
 TTYPESTVGTLM SKLRELGRDAADLLKASSVFKINLDGNGQEAYASSCNSGTSYNSI  
 SSVVSR

SEQID No:123

MWTPTEEEKYGVVICSFRGSPVQGLVLEIGETVQILEKCEGWYRGVSTKKPNVKGIFPA  
 NYIHLKKAIVSNRGQYETVVPLEDIVTEVTATLQEWASLWKQLYVKHKVDLFYKLRHV  
 MNELIDLRRQLLSGHLTQDQVREVKRHITVRLDWGNEHLGLDLVPRKDFEVVDSQISV  
 SDLYKMHLSSRQSVQQSTSQVD TMRPRHGETCRMPVPHHFFLSLSKSTYNTIGEDTDV  
 FFSLYDMREGKQISERFLVRLNKNGGPRNPEKIERMCALFTDLSSKDMKRDLYIVAHVIR  
 IGRMLLND SKKGPPHLHYRRPYGCAVLSILDVLQSLTEVKEEKDFVLKVYTCNNESEWS  
 QIHENIIRKSSAKYSAPSASHGLIISLQLLRGDMEQIRRENPMIFNRGLAITRKLGFDPVIM  
 PGDIRNDLYLTLEKGD FERGGSVQKNIEVTMYVLYADGEILKDCISLGSGEPNRSSYHS  
 FVLYHSNSPRWGEIILPIPIDRFRGSHLRFEFRHCSTKDKGEKKLFGFAFSTLMRDDGT  
 TLSDDIHELYVYKCDENSTFNNHALYLGLPCKEDYNGCPNIPSSLIFQRSTKESFFISTQ  
 LSSTKLTQNVDLLALLKWKAFPD RIMDVLGRLRHVS GEEIVKFLQDILDTL FVILDDNTEK  
 YGLLVFQSLVFIINLLRDIKYFHRPVM DTYIQKH FAGALAYKELIRCLKWYMDCSAELIR

QDHIQEAMRALEYLFKFIVQSRILYSRATCGMEEEQFRSSIQELFQSIRFVLSLDSRNSET  
 LLFTQAALLNSFPTIFDELLQMFTVQEVAFVRGTLGSMPSTVHIGQSMDEVVKLQSIART  
 VDSRLFSFSESRRILLPVVLHHIHLHLRQQKELLICSGILGSIFSIVKTSSLEADVMEEVEM  
 MVESLLDVLLQTLLTIMSKSHAQEAVRGQRCPQCTAEITGEYVSCLLSLLRQMCDTHFQ  
 HLLDNFQSKDELKEFLLKIFCVFRNLMKMSVFPRDWMVMRLLTSNIIVTTVQYLSSALHK  
 NFTETDFDFKVWNSYFSLAVLFINQPSLQLEITSKRKKILDKYGDMRVMMAYELFSMW  
 QNLGEHKKIHFIPGMIGPFLGVTLPQPEVRNIMIPIFHDMMDWEQRKNGNFKQVEAELID  
 KLDSMVSEGKGDESYRELFSLLTQLFGPYPSLLEKVEQETWRETGISFVTSVTRLMERL  
 LDYRDCMKGEETENKKIGCTVNLNMFYKSEINKEEMYIRYIHKLCDMHLQAENYTEAAF  
 TLLLYCELLQWEDRPLREFLHYPSTEWQRKEGLCRKIIHYFNKGKSWFEGIPLCRELA  
 CQYESLYDYQSLSWIRKMEASYDNIMEQQRLEPEFFRVGFYGRKFPFFLRNKEYVCR  
 GHDYERLEAFQQRMLSEFPQAVAMQHNPNDAILQCDAAQYLQIYAVTPIPDYVDVLQ  
 MDRVDPDRVKSFYRVNNVRKFRYDRPFHKGPKDKENEFKSLWIERTTLTLTHSLPGISR  
 WFEVERRELVEVSPLNAIQVVENKNQELRSLISQYQHKQVHGNINLLSMCLNGVIDAA  
 VNGGIARYQEAFFDKDYINKHPGDAEKITQLKELMQEQVHVLGVGLAVHEKFVHPEMR  
 PLHKKLIDQFQMMRASLYHEFPGLDKLSPACSGTSTPRGNVLASHSPMSPESIKMTHR  
 HSPMNLMTGTGRHSSSSSLSSHASSEAGNMVMLGDGSMGDAPEDLYHHMQLAYPNPRY  
 QGSVTNVSVLSSSSQASPSSSSLSTHSAPSQMITSAPSSARGSPSLPDKYRHAREMML  
 LLPTYRDRPSSAMYPAAILENGQPPNFQRALFQQVVGACKPCSDPNLSVAEKGHYSLH  
 FDAFHPLGDTPPALPARTLRKSPHPIASPTSPQSGLDGSNSTLSGSASSGVSSLSE  
 SNFGHSSEAPPRTDTMDSMPSQAWNADEDLEPPYLPVHYSLSSESAVLDSIKAQPCRSH  
 SAPGCVIPQDPMDDPALPPKPYHPRLPALHDEGVLLREETERPRGLHRKAPLPPGSA  
 KEEQARMAWEHGRGEQ

SEQID No:124

MAATFFGEVVKAPCRAGTEDEEEEEEGRRETPEDREVRLQLARKREVRLRRQTKTSL  
 EVSLLEKYPCSKFIIAIGNNAVAFLSSFVMNSGVWEEVGCALWNEWCRTTDTTHLSST  
 EAFCVFYHLKSNPSVFLCQCSCYVAEDQQYQWLEKVFGSCPRKNMQITILTCRHVTDY  
 KTSESTGSLPSPFLRALKTONFKDSACCPILLEQPNIVHDLPAAVLSYCQVWKIPAILYLC  
 YTDVMKLDLITVEAFKPILSTRSLKGLVKNIPQSTEILKKLMTTNEIQSNIYT

SEQID No:125

MSWVQATLLARGLCRAWGGTCGAALTGTSISQVPRRLPRGLHCSAAAHSSSEQSLVPS  
 PPEPRQRPTKALVPFEDLFGQAPGGERDKASFLQTVQKFAEHSVRKRGHIDFIYLALRK



MREYGVERDLAVYNQLLNIFPKEVFRPRNIIQRIFVHYPRQQECGIAVLEQMENHGVMP  
 NKETEFLLIQIFGRKSYPMMLKLVRLKLWFPRFMNVNPFVPRDLPQDPVELAMFGLRHM  
 EPDLSARVTIYQVPLPKDSTGAADPPQPHIVGIQSPDQQAALARHNPARPVFVEGPFSL  
 WLRNKCYYYHILRADLLPPEEREVEETPEEWNLYYPMQLDLEYVRSGWDNYEFDINEV  
 EEGPVFAMCMAGAHDQATMAKWIQGLQETNPTLAQIPVVFRLAGSTRELQTSSAGLEE  
 PPLPEDHQEEDDNLQRQQGQS

SEQID No:126

MQAHELFRYFRMPELVDFRQCCTLPTNTLMGFGAFSRRLTTFWRPRHPKPLKPPWHL  
 SMQSVEVAGSGGARRSALLDSDEPLVYFYDDVTTLYEGFQRGIQVSNNGPCLGSRKP  
 DQPYEWLSYKQVAELSECIGSALIQKGFKTAPDQFIGIFAQNRPEWVIIQQGCFAYSMVI  
 VPLYDTLGNEAITIYVNKAELSLVFVDKPEKAKLLLEGVENKLIPGLKIIVVMDSYGSELVE  
 RGQRCGVEVTSMKAMEDLGRANRRKPKPPAPEDLAVICFTSGTTGNPKGAMVTHRNIV  
 SDCSAFVKATENTVNPCPDDTLISFLPLAHMFERVVECVMLCHGAKIGFFQGDIRLLMD  
 DLKVLQPTVFPVPRLLNRMFDRIFGQANTTVKRWLLDFASKRKEADVRSIGIRNNSLW  
 DRLIFHKVQSSLGGRVRLMVTGAAPVSATVLTFLRAALGCQFYEGYGQTECTAGCCLT  
 MPGDWTTGHVGAPMPCNLIKLGWQLEEMNYMASEGEGEVCVKGPNVFQGYLKDPAK  
 TAEALDKDGWLHTGDIGKWLPNGTLKIIDRKKHIFKLAQGEYIAPEKIENIYMRSEPVAQV  
 FVHGESLQAFLIAIVVPDVETLCSWAQKRGFEGSFEELCRNKDVKKAILEDMMVRLGKDS  
 GLKPFEQVKGITLHPELFSIDNGLLTPTMKAKRPELRNYFRSQIDDLYSIIKV

SEQID No:127

MPSASCDTLLDDIEDIVSQEDSKPQDRHFVRKDVVPKVRRRNTQKYLQEEENSPPSDS  
 TIPGIQKIWIRTWGCSHNSDGEYMAGQLAAYGYKITENASDADLWLLNSCTVKNPAED  
 HFRNSIKKAQEENKKIVLAGCVPAQPRQDYKGLSIIQVQQIDRVVEVVEETIKGHSVR  
 LLGQKKDNGRRLGGARLDLPKIRKNPLIEIISISTGCLNACTYCKTKHARGNLASYPIDEL  
 VDRAKQSFQEGVCEIWLTSED TGAYGRDIGTNLPTLLWKLVEVIPEGAMLRLGMTNPPY  
 ILEHLEEMAKILNHPRVYAFLHIPVQSASDSVLMEMKREYCVADFKRVDLKEKVPGITI  
 ATDIICGFPGETDQDFQETVKLVEEYKFPSLFINQFYPRPGTPAAKMEQVPAQVKKQRT  
 KDLSRVFHSYSPYDHKIGERQQVLVTEESFDSKFYVAHNQFYEQVLVPKNPAFMGKMV  
 EVDIYESGKHFMKGQPVSDAKVYTSPISKPLAKGEVSGLTKDFRNLGNQLSSGSHTS  
 AASQCDSASSRMVLPMPRLHQDCALRMSVGLALLGLLFAFFVKVYN

SEQID No:128

MGGTTSTRRTFEADENENITVVKGIRLSENVIDRMKESSPSGSKSQRYSGAYGASVS  
DEELKRRVAEELALEQAKKESEDQKRLKQAKELDRERAAANEQLTRAILRERICSEEER  
AKAKHLARQLEEKDRVLKKQDAFYKEQLARLEERSSEFYRVTTTEQYQKAAEEVEAKFK  
RYESHVPCADLQAKILQCYRENTHTQTLKCSALATQYMHCNVNHAKQSMLEKGG

SEQID No:129

MALAARLLPQFLHSRSLPCGAVRLRTPAVAEVRLPSATLCYFCRCRLGLGAALFPR SAR  
ALAASALPAQGSRWVPLSSPGLPAAFASFPACPQRSYSTEEKPQQHQKTKMIVLGF SN  
PINWVRTRIKAFLIWAYFDKEFSITEFSEGAKQAFAHVSKLLSQCKFDLLEELVAKEVLHA  
LKEKVTSLPDNHKNALANIDEIVFTSTGDISIYYDEKGRKFVNILMCFWYLTSANIPSETL  
RGASVFQVKLGNQNVETKQLLSASYEFQREFTQGVKPDWTIARIEH SKLLE

SEQID No:130

MRASLLLSVLRPAGPVAVGISLGFTLSLLSVTWVEEPCGPGPPQPGDSELP PRGNTNA  
ARRPNSVQPGAEREKPGAGEGAGENWEPRVLPYHPAQPGQAAKKAVRTRYISTELGI  
RQRLLVAVLTSQTTLPTLGVAVNRTLGHRLERVVFLTGARGRRAPPGMAVVTLGEERPI  
GHLHLALRHILLEQHGDDFDWFFLVDPDTTYTEAHGLARLTGHLSLASAAHLYLGR PQDFI  
GGEPTPGRYCHGGFGVLLSRMLLQQLRPHLEGCRNDIVSARPDEWLGR CILDATGVG  
CTGDHEGVHYSHLELSPGEPVQEGDPHF RSALTAHPVRDPVHMYQLHKAFARAELE R  
TYQEIQELQWEIQNTSHLAVDGDRAAAWPVGIPAPSRPASRFEVLRWDYFTEQHAFSC  
ADGSPRCPLRGADRADVADVLTGTALEELNRRYHPALRLQKQQLVNGYRRFD PARGME  
YTLDLQLEALTPQGGRRPLTRRVQLLRPLSRVEILPVPYVTEASRLTVLLPLAAAERDLA  
PGFLEAFATAALEPGDAAAALTLLLLYEPRQAQRVAHADVFAPVKAHVAELERRFP GAR  
VPWLSVQTAAPSPLRLMDLLSKKHPLDTLFLLAGPDTVLT PDFLNRCRMHAISGWQAFF  
PMHFQAFHPAVAPPQGPPELGRDTGRFDRQAASEACFYNSDYVAARGRLAAASEQ  
EEELLES LDVYELFLHFSSLHVLRAVEPALLQRYRAQTCSARLSEDLYHRCLOQSVLEGL  
GSRTQLAMLLFEQEQQNST

SEQID No:131

MKLKLNKVF LAYFLVSIAGLLYALVQLGQPCDCLPPLRAAAEQLRQKDLRISQLQAE LRR  
PPPAPAQPPPEALPTIYVVTPTYARLVQKAELVRLSQTLSLVPRLHWLLVEDAEGPTPL  
VSGLLAASGLLFTHLVLT PKAQRLREGE PGWVHPRGVEQRNKALDWLRGRGGAVGG  
EKDPPPPGTQGVVYFADDDNTYSRELSEEMRWTRGVSVWPVGLVGGLRFEGPQVQD

GRVVGHTAWEPSRPFVDMAGFAVALPLLLDKPNAQFDSTAPRGHLESSLLSHLVDP  
KDLEPRAANCTRVLVWHTRTEKPKMKQEEQLQRQGRGSDPAIEV

SEQID No:132

MAAPRAGRGAGWSLRAWRALGGIRWGRRPRLTPDLRALLTSGTSDPRARVTYGTPSL  
WARLSVGVTEPRACLTSGTPGPRAQLTAVTPDTRTREASENSGTRSRAWLAVALGAG  
GAVLLLLWGGGRGPPAVLAAVPSPPPASPRSQYNFIADVVEKTAPAVVYIEILDRHPFLG  
REVPISNGSGFVVAADGLIVTNAHVADRRRVRVRLLSGDTYEAVVTAVDPVADIATLRI  
QTKEPLPTLPLGRSADVRQGEFVAMGSPFALQNTITSGIVSSAQRPARDLGLPQTNVE  
YIQTDAIDFGNSGGPLVNLDGEVIGVNTMKVTAGISFAIPSDRLREFLHRGEKKNSSSGI  
SGSQQRRYIGVMMLTSPSILAEQLREPSFPDVQHGVLIHKVILGSPAHRAGLRPGDVIL  
AIGEQMVQNAEDVYEAVRTQSQLAVQIRRGRETTLTYVTPEVTE

SEQID No:133

MTQLFLWEYGDHLHFGPNQRPAPCYDPCEAVLVESIPEGLDFPNASTGNPSTSQAWLG  
LLAGAHSSLDIASFYWTLTNNDTHTQEPSAQQGEEVLRQLQTLAPKGVNVRIAVSKPSG  
PQPQADLQALLQSGAQVRMVDQMQLTHGVLHTKFWVVDQTHFYLG SANMDWRSLTQ  
VKELGVVMYNCSC LARDLT KIFEAYWFLGQAGSSIPSTWPRFYDTRYNQETPMEICLNG  
TPALAYLASAPPPLCPSGRTPDLKALLNVVDNARSFIYVAVMNYLPTLEFSHPHRFWPAI  
DDGLRRATYERGVKVRLLISCWGHSEPSMRAFLLSLAALRDNHTHSDIQVKLFVVPAD E  
AQARIPYARVNH NKYMVTERATYIGTSNWSGNYFTETAGTSLLVTQNGRGGLRSQLEAI  
FLRDWDSPYIHDLDTSADSVGNACRL

SEQID No:134

MRYFLLRPETLFLLCISLALWSYFFHTDEVKTIVKSSRDAVKMVKGKVAEIMQNDR LGGL  
DVLEAEFSKTWEFKNHNNAVYSIQGRRDHMEDRFEVLTD LANKTHPSIFGIFDGHGGE  
GGIRGAALRFFPTLSTLQVQSGQLTGAPRWPLVFTRISERDLDPGLCRGGYARKGGG  
ALTSPLRPGGLRGADVLLLD SFVCGSSGSRR

SEQID No:135

MEKQPQNSRRGLAPREVPPAVGLLLIMALMNTLLYLCLDHFFIAPRQSTVDPTHCPYGH  
FRIGQMKNCS PWLSCEELRTEVRQLKRVGEGAVKRVFLSEWKEHKVALS QLT SLEMKD  
DFLHGLQMLKSLQGTHVVTLLGYCEDDNTMLTEYHPLGSLSNLEETLNLSKYQNVNTW  
QHRLELAMDYVSIINYLHHSPVGTRVMCDSNDLPKTL SQYLLTSNFSILANDLDALPLVN

HSSGMLVKCGHRELHGDFVAPEQLWPYGEDVPFHDDLMPHYDEKIDIWKIPDISSFLLG  
HIEGSDMVRFHFLFDIHKACKSQTPSERPTAQDVLETYQKVLDTLRDAMMSQAREML

SEQID No:136

MQRAGSSSGRGECDISGAGRLGLEEAARLSCAVHTSPGGGRRPGQAAGMSAKERPK  
GKVIKDSVTLLPCFYFVELPILASSVVSLEYFLELTDVFKPVHSGFSCYDRSLSMPIEPTQ  
EAIPFLMLLSLAFAGPAITIMVGEGILYCCLSKRRNGVGLPNINAGGCNFSFLRRAVRF  
VGVHVFGLCSTALITDIIQLSTGYQAPYFLTVCKPNYTSNLVSCCKENSYIVEDICSGSDLT  
VINSGRKSFPSQHATLAFAAVYVSMYFNSTLTDSKLLKPLLVTFTIICGIIICGLTRITQY  
KNHPVDVYCGFLIGGGIALYLGLYAVGNFLPSDESMFQHRDALRSLTDLNQDPNRLLSA  
KNGSSSDGIAHTEGILNRNHRDASSLTNLKRANADVEITPRSPMGKENMVTFSNTLPRA  
NTPSVEDPVRRNASIHASMDSARSKQLLTQWKNKNESRKLSLQVIEPEPGQSPPRSIE  
MRSSSEPSRVGVNGDHHGPGNQYLKIQPGAVPGCNNSMPGGPRVSIQSRPGSSQLV  
HIPEETQENISTSPKSSSARAKWLKAAEKTACNRNSNSQPRIMQVIAMSKQQGVLLQSSP  
KNTGEGSTVSGTGSIRYKTLTDHEPSGIVRVEAHPENNRPIIQIPSTEGEGSGSWKWKAP  
EKGSLRQTYELNDLNRDSESCESLKDSFGSGDRKRSNIDSNEHHHHGITTIRVTPVEGS  
EIGSETLSISSSRDSTLRRKGNILIPERSNSPENTRNIFYKGTSPTRAYKD

SEQID No:137

MLTTLKPFGSVSVESKMNNKAGSFFWNLRQFSTLVSTSRMTMLCCLGLCKPKIVHSNW  
NILNNFHNRMQSTDIIRYLFQDAFIFKSDVGFQTKGISTLTALRIERLLYAKRLFFDSKQSL  
VPVDKSDDELKKVNLNHEVSNEDVLTKETKPNRISSRKLSSEECNSLSDVLDAFSKAPTF  
PSSNYFTAMWTIAKRLSDDQKRFEKRLMFSHPAFNQLCEHMMREAKIMQYKYLLFSHL  
AIVKLGIPQNTILVQTLLRVTQERINECDEICLSVLSTVLEAMEPCKNVHVLRTGFRILVDQ  
QVWKIEDVFTLQVVMKCIGKDAPIALKRKLEMKALRELDRLFVLSQHMFEVLAAMNHR  
SLILLDECSKVVDNIHGCPLRIMINILQSCKDLYHNLDLFGKLADYVAATFDIWKFRKVL  
FILILFENLGFRPVGLMDLFMKRIVEDPESLNMKNILSILHTYSSLNHVYKCQNKEQFVEV  
MASALTGYLHTISSENLLDAVYSFCLMNYFPLAPFNQLLQKDIISELLTSDDMKNAYKLHT  
LDTCLKLDDTVYLRDIALSLPQLPRELPSSHTNAKVAEVLSSLLGGEGHFSKDVHLPHNY  
HIDFEIRMDTNRNQVLPLSDVDTTSATDIQRVAVLCVSR SAYCLGSSHPRGFLAMKMRH  
LNAMEGFHVILVNNWEMDKLEMEDAVTFLKTKIYSVEALPVAAVNVQSTQ

SEQID No:138

RVYADAPAKLLLPPPAAWDLAVRLRGAEAAASERQVYSVTMKLLLLHPAFQSCLLLTLG

LWRTTPEAHASSLGAPAIASAASFLQDLIHRYGEGDSLTLQQLKALLNHLDVGVGRGNVT  
 QHVQGHRNLSTCFSSGDLFTAHNFSEQSRIGSSELQEFCPTILQQLDSEACTSENQEN  
 EENEQTEEGRPSSAVEVWGYGLLCVTVISLCSLLGASVVPFMKKTFFYKRLLLYFIALAIGTL  
 YSNALFQLIPEAFGFNPLEDYYVSKSAVVFGGFYLFFFTEKILKILLKQKNEHHHGHSHYA  
 SESLPSKKDQEEGVMEKLQNGDLDHMIPQHCSSELDGKAPMVDEKVIVGSLSVQDLQA  
 SQSACYWLKGVRYSDIGTLAWMITLSDGLHNFIDGLAIGASFTVSVFQGISTSVAILCEE  
 PHELGDVFILLNAGMSIQQALFFNFLSACCCYLGLAFGILAGSHFSANWIFALAGGMFLYI  
 SLADMFPENNEVCQEDERKGSILIPFIIQNLGLLTGFTIMVVLTMYSGQIQIG

SEQID No:139

MAAEWASRFWLWATLLIPAAAVYEDQVGKFDWRQQYVGKVKFASLEFSPGSKKLVA  
 TEKNVIAALNSRTGEILWRHVDKGTAEGAVDAMLLHGQDVITVSNGGRIMRSWETNIGG  
 LNWEITLDSGSFQALGLVLGLQESVRYIAVLKKTTLALHHLSSGHLKWVEHLPESDSIHYQ  
 MVYSYSGSVVWALGVVPFSHVNIKFNVEDGEIVQQVRVSTPWLQHLGACGVVDEA  
 VLVCPDPSSRSLQTLALETWELRQIPLQSLDLEFGSGFQPRVLPQTQPNPVDASRAQFF  
 LHLSPSHYALLQYHYGTLSLLKNFPQTALVSFATTGEKTVAAVMACRNEVQKSSSSSEDG  
 SMGSFSEKSSSKDSLACFNQTYTINLYLVETGRRLDTTITFSLEQSGTRPERLYIQVFLK  
 KDDSVGYRALVQTEDHLLLFLQQLAGKVVLWSREESLAEVVCEMVDLPLTGAQAELE  
 GEFGKKADGLLGMFLKRLSSQLILLQAWTSHLWKMFDYDARKPRSQIKNEINIDTLARDEF  
 NLQKMMVMVTASGKLFGIESSSGTILWKQYLPNVKPDSSFKLMVQRTTAHFPHPPQCT  
 LLVKDKESGMSSLYVFNPIFGKWSQVAPPVLKRPIQLSLLPVMDQDYAKVLLLIDDEYK  
 VTAFPATRNVLRLHELAPSIFFYLVDAAEQGRLCGYRLRKDLTTELSWELTIPPEVQRIV  
 KVKGKRSEHVSQGRVMGDRSVLYKSLNPNLLAVVTESTDAHHERTFIGIFLIDGVTG  
 RIIHSSVQKKAKGPVHIVHSENWVYQYWNTKARRNEFTVLELYEGTEQYNATAFSSLD  
 RPQLPQVLQQSYIFPSSISAMEATITERGITSRHLLIGLPSGAILSLPKALLDPRRPEIPTE  
 QSREENLIPYSPDVQIHAERFINYNQTVSRMRGIYTAPSGLESTCLVVAYGLDIYQTRVY  
 PSKQFDVLKDDYDYVLISSVLFGLVFATMITKRLAQVKLLNRAWR

SEQID No:140

MAKVSELYDVTWEEMRDKMRKWREENSRNSEQIVEVGEELINEYASKLGDDIWIIYEQV  
 MIAALDYGRDDLALFCLQELRRQFPGSHRVKRLTGMRFEAMERYDDAIQLYDRILQEDP  
 TANTAARKRKIAIRKAQGKNVEAIRELNEYLEQFVGDEAWHELAELYINEHDYAKAAFCL  
 EELMMTNPHNHLVCQQAQYAEVKYTQGGLENLELSRKYFAQALKLNNRNMRALFGLYMS

ASHIASNPKASAKTKKDNMKYASWAASQINRAYQFAGRSKKETKYSLKAVEDMLETLQI  
TQS

SEQID No:141

MWSIGAGALGAAALALLANTDVFLSKPQKALEYLEDIDLKTLEKEPRTFKAKELWEKN  
GAVIMAVRRPGCFLCREEAADLSSLKSMLDQLGVPLYAVVKEHIRTEVKDFQPYFKGEI  
FLDEKKKFYGPQRRKMMFMGFIRLGVWYNFFRAWNGGFSGNLEGEFILGGVFVVG  
GKQGILLEHREKEFGDKVNLLSVLEAAKMIKPQTLASEKK

SEQID No:142

MTLIEGVGDEVTVLFSVLACLLVLALAWVSTHTAEGGDPLPQPSGTPTPSQPSAAMAAT  
DSMRGEAPGAETPSLRHRGQAAQPEPSTGFTATPPAPDSPQEPLVRLKFLNDSEQVA  
RAWPHDTIGSLKRTQFPGREQQVRLIYQGQLGDDTQTLGSLHLPNCVLHCHVSTRV  
GPPNPPCPPGSEPGPSGLEIGSLLLPLLLLLLLLLLWYCQIQYRPFPLTATLGLAGFTLLL  
SLLAFAMYRP

SEQID No:143

MASGSNWLSGVNVVLVMAYGSLVFVLLFIFVKRQIMRFAMKSRRGPHVPVGHNAPKDL  
KEEIDIRLSRVQDIKYEPQLLADDDARLLQLETQGNQSCYNLYRMKALDAIRTSEIPFHS  
EGRHPRSLMGKNFRSYLLDLRNTSTPFKGVRKALIDTLDDGYETARYGTGVFGQNEYL  
RYQEALSELATAVKARIGSSQRHHQSAAKDLTQSPEVSPTTIQVTYLPSSQKSKRAKHF  
LELKSFKDNYNTLESTL

SEQID No:144

MTARGLALGLLLLLLCPAQVFSQSCVWYGECGIAYGDKRYNCEYSGPPKPLPKDGYDL  
VQELCPGFFFFGNVSLCCDVRLQTLKDNLQLPLQLFLSRCPSCFYNLLNLFCELTCSPRQ  
SQFLNVTATEDYVDPVTNQTKTNVKELQYYVGQS FANAMYNACRDVEAPSSNDKALGL  
LCGKDADACNATNWIEYMFNKNNGQAPFTITPVFSDFPVHGMEPMNNATKGCDESVD  
EVTAPCSCQDCSIVCGPKPQPPPPAPWTILGLDAMYVIMWITYMAFLLVFFGAFFAWW  
CYRKRYFVSEYTPIDSNIAFSVNASDKGEASCCDPVSAAFEGCLRRLFTRWGSFCVRN  
PGCVIFFSLVFITACSSGLVFVRVTNPVDLWSAPSSQARLEKEYFDQHFGPFFRTEQLII  
RAPLTDKHIYQPYPGADVFPGPPLDIQILHQVLDLQIAIENITASYNETVTLQDICLAPL  
SPYNTNCTILSVLNYFQNSHSVLDHKKGDDFFVYADYHTHFLYCVRAPASLNDTSLLHD  
PCLGTFGGPVFPWLVLGGYDDQNYNNATALVITFPVNNYYNDTEKLQRAQAWKEFIN

FVKNYKNPNLTISFTAERSIEDELNRESDSVFTVVISYAIMFLYISLALGHIKSCRRLVD  
 SKVSLGIAGILIVLSSVACSLGVFSYIGLPLTLIVIEVIPFLVLAVGVDNIFILVQAYQRDERL  
 QGETLDQQLGRVLGEVAPSMFLSSFSETVAFFLGALSVMMPAVHTFSLFAGLAVFIDFLL  
 QITCFVSLGLDIKRQEKNRLDIFCCVRGAEDGTSVQASESCLFRFFKNSYSPLLLKDW  
 MRPIVIAIFVGVLSFSIAVLNKVDIGLDQSLSMPPDDSYMVDYFKSISQYLHAGPPVYFVLE  
 EGHDTSSKGMNMVCGGMGCNNDSLVQQIFNAAQLDNYTRIGFAPSSWIDDYFDWVK  
 PQSSCCRVDNITDQFCNASVVDPAVRCRPLTPEGKQRPQGGDFMRFLPMFLSDNPN  
 PKCGKGGHAAYSSAVNILLGHGTRVGATYFMTYHTVLQTSADFIDALKKARLIASNVTT  
 MGINGSAYRVFPYSVFYVFEYQYLTIIDDTIFNLGVSLGAIFLVTMVLGCELWSAVIMCA  
 TIAMVLVNMFGVMWLWGISLNAVSLVNLVMSCGISVEFCSHITRAFTVSMKGSERVERAE  
 EALAHMGSSVFSGITLTKEGIVVLAFAKSQIFQIFYFRMYLAMVLLGATHGLIFLPVLLSY  
 IGPSVKNKAKSCATEERYKGTERERLLNF

SEQID No:145

MSGCGLFLRTTAAARACRGLVVSTANRRLLRTSPPVRAFAKELFLGKIKKKEVFPFPEV  
 SQDELNEINQFLGPVEKFFTEEVDNRKIDQEGKIPDETLEKLKSLGLFGLQVPEEYGGGLG  
 FSNTMYSRLGEIISMDGSITVTAAHQAIQGLKGIILAGTEEQKAKYLPKLASGEHIAAFCLT  
 EPASGSDAASIRSRATLSEDKKHILNGSKVWITNGGLANIFTVFAKTEVVDSGDSVKDK  
 ITAFIVERDFGGVTNGKPEDKLGIRGSNTCEVHFENTKIPVENILGEVGDGFKVAMNINLS  
 GRFSMGSVVAGLLKRLIEMTAEYACTRKQFNKRLSEFGLIQEKFALMAQKAYVMESMT  
 YLTAGMLDQPGFPDCSIEAAMVKVFSSEAAWQCVSEALQILGGLGYTRDYPYERILRDT  
 RILLIFEGTNEILRMYIALTGLQHAGRILTTRIHELKQAKVSTVMDTVGRRLRDSLGRTVDL  
 GLTGNHGVVHPSLADSANKFEENTYCFGRTVETLLLRFGKTIMEEQVLKRVANILINLY  
 GMTAVLSRASRSIRIGLRNHDHEVLLANTFCVEAYLQNLFSLSQLDKYAPENLDEQIKKV  
 SQQILEKRAYICAHPLDRTC

SEQID No:146

LERRWRRRRREAGAGAEAAAGSARPLGRQAAAARGSSPEAGAAAMAESIIIRVQSPDGV  
 KRITATKRETAATFLKKVAKEFGFQNNGFSVYINRNKTGEITASSNKSLLKIKHGDLLF  
 LFPSSLAGPSSEMETSVPFGFKVFGAPNVVEDEIDQYLSKQDGKIYRSRDPQLCRHGPL  
 GKCVHCVPLEPDEDYLNHLEPPVKHMSFHAYIRKLTGGADKGGKFVALENISCKIKSGC  
 EGHLPWPNGICTKCQPSAITLNRQKYRHVDNIMFENHTVADRFLDFWRKTGNQHFQYL  
 YGRYTEHKDIPLGIRAEVAAIYEPPIGTQNSLELLEDPKAEVVDEIAAKLGLRKVGWIFT  
 DLVSEDTRKGTVRYSRNKDTYFLSSEECITAGDFQNKHPNMCRLSPDGHFGSKFVTAV

ATGGPDNQVHFEGYQVSNQCMALVRDECLLPCKDAPELGYAKESSEQYVPDVFYKD  
 VDKFGNEITQLARPLPVEYLIIDITTTFPKDPVYTFSSISQNPFPPIENRDVLGETQDFHSLAT  
 YLSQNTSSVFLDTISDFHLLLFLVTNEVMPLQDSISLLLEAVRTRNEELAQTWKRSEQWA  
 TIEQLCSEYPHPLPRHPVAGAGEQPTLHSSPLPVVPWIPHPAASWQVPSAMQRVETRP  
 PCQARGRLR

SEQID No:147

MATAGGGSGADPGSRGLLRLLSFCVLLAGLCRGNSVERKIYIPLNKTAPCVRLLNATHQI  
 GCQSSISGDTGVIHVVEKEEDLQWVLTGDPNPPYMVLLSKHFTRDLMEKLGRTSRIA  
 GLAVSLTKPSPASGFSPSVQCPNDGFGVYSNSYGPEFAHCREIQWNSLGNGLAYEDFS  
 FPIFLEDENETKVIKQCYQDHNLSQNGSAPTFLCAMQLFSHMHAVISTATCMRRSSIQ  
 STFSINPEIVCDPLSDYNVWSMLKPINTTGTLPDDRVAATRLDSRSFFWNVAPGAE  
 SAVASFVTQLAAAEALQKAPDVTTLPNRNMFVFFQGETFDYIGSSRMVYDMEKGKFPV  
 QLENVDSFVELGQVALRTSLELWMHTDPVSQKNESVRNQVEDLLATLEKSGAGVPAVI  
 LRRPNQSQPLPPSSLQRFLRARNISGVVLADHSGAFHNKYYQSIYDTAENINVSYPEWL  
 SPEEDLNFTDTAKALADVATVLGRALYELAGGTNFSDTVQADPQTVTRLLYGFLIKAN  
 NSWFQSILRQDLRSYLGDGPLQHYIAVSSPTNTTYVVQYALANLTGTVVNLTREQCQDP  
 SKVPSENKDLYEYSWVQGPLHSNETDRLPRCVRSTARLARALSPAFELSQWSSTEYST  
 WTESRWKDIRARIFLIASKELELITLVGFGILIFSLIVTYCINAKADVLFIAPREPGAVSY

SEQID No:148

MPSAKQRGSKGGHGAASPSEKGAHPSGGADDVAKKPPPAPQQPPPPAPHPQQHPQ  
 QHPQNQAHGKGGHRRGGGGGGGKSSSSSSASAAAAAAAASSSASCSRRLGRALNFLF  
 YLALVAAAFAFGWCVHHVLEEVQQVRRSHQDFSRQREELGQGLQGVEQKVQSLQATF  
 GTFESILRSSQHKQDLTEKAVKQGESEVSRISEVLQKLQNEILKDLSDGIHVVKDARERD  
 FTSLENTVEERLTELTKSINDNIAIFTEVQKRSQKEINDMKAKVASLEESEGNKQDLKALK  
 EAVKEIQTSAKSREWDMEALRSTLQTMESDIYTEVRELVSLLKQEQQAFKEAADTERLAL  
 QALTEKLLRSEESVSRLPEEIRRLEEELRQLKSDSHGPKEDGGFRHSEAFEALQQKSQ  
 GLDSRLQHVEDGVLSMQVASARQTESLESLLSKSQEHEQRLAALQGRLEGLGSSEAD  
 QDGLASTVRSLGETQLVLYGDVEELKRSVGELPSTVESLQKVQEQQVHTLLSQDQAQAA  
 RLPPQDFLDRLSSLDNLKASVSQVEADLKMLRTAVDSLVAYSVKIETNENNLESAGLL  
 DDLRNDLDRLFVKVEKIHEKV



SEQID No:149

MFRNQYDNDVTWSPQGRIHQIEYAMEAVKQGSATVGLKSKTHAVLVALKRAQSELAA  
 HQKKILHVDNHIGISIAGLTADARLLCNFMRQECLDSRFVDRPLPVSRLVSLIGSKTQIP  
 TQRYGRRPYGVGLLIAGYDDMGPHIFQTCPSANYFDCRAMSIGARSQSARTYLERHMS  
 EFMECNLNELVKHGLRALRETLPAEQDLTTKNV SIGIVGKDLEFTIYDDDDVSPFLEGLE  
 ERPQRKAQPAQPADEPAEKADEPMEH

SEQID No:150

SSIGTGYDLSASTFSPDGRVFQVEYAMKAVENTSSTAIGIRCKDGVVFGVEKLVLSKLYEE  
 GSNKRLFNVDHRVGMAGVAGLLADARSLADIAREEASNFRSNFGYNIPLKHLADRVAMY  
 VHAYTLYSAVRPFGCSFMLGSSVNDGAQLYMIDPSGVSYGYWGCAIGKARQAAKTEI  
 EKLOMKEMTCRDIVKEVAKIIVHDEVKDKAFELELSWVGELTNGRHEIVPKDIREEA EK  
 YAKESLKEEDESDDDNM

SEQID No:151

MSRRYDSRTTIFSPEGRLYQVEYAMEAIGHAGTCLGILANDGVLLAAERRNIHKLLDEVF  
 FSEKIYKL NEDMACSVAGITSDANVLTNELRLIAQRYLLQYQEPICEQLVTALCDIKQAY  
 TQFGGKRPFPGVSLLYIGWDKHYGFQLYQSDPSGNYGGWKATCIGNNSAAAVSMLKQD  
 YKEGEMTLKSALALAIKVLNKTMDVSKLSAEKVEIATLTRENGKTVIRVLKQKEVEQLIKK  
 HEEEEAKAEREKKEKEQKEKDK

SEQID No:152

MSRGSSAGFDRHITIFSPEGRLYQVEYAFKAINQGGLTSVAVRGKDCAVIVTQKKVPDK  
 LLDSSSTVTHLFKITENIGCVMTGMTADSR SQVQRARYEAANWKYKYGYEIPVDMLCKRI  
 ADISQVYTQNAEMRPLGCCMILIGIDEEQG PQVYKCDPAGYYCGFKATAAGVKQTESTS  
 FLEKKVKKKFDWTFEQTVETAITCLSTVLSIDFKPSEIEVG VVTVENPKFRILTEAEID AHL  
 VALAERD

SEQID No:153

MLSSTAMYSAPGRDLGMEPHRAAGPLQLRFSPYVFNGGTILAIAGEDFAIVASDTRLSE  
 GFSIHTRDSPKCYKLTDKTVIGCSGFHGDCLTLTKIIEARLKMYSNNKAMTTGAIAAM  
 LSTILYSRRFFPYVYNIIGGLDEEGKGAVYSFDPVGSYQRDSFKAGGSASAM LQPLLD  
 NQVGFKNMQNVEHVPLSLDRAMRLVKDVFISAAERDVYTG DALRICIVTKEGIREETVSL  
 RKD

SEQID No:154

MEYLIGIQGPDYVLVASDRVAASNIVQMKDDHDKMFKMSEKILLLCVGEAGDTVQFAEYI  
QKNVQLYKMRNGYELSPTAAANFTRRNLDCLRSRTPYHVNLLLAGYDEHEGPALYYM  
DYLAALAKAPFAAHGYGAFLTLSILDYRYTPTISRERAVELLRKCLEELQKRIFILNLPFTSV  
RIIDKNGIHDLDNISFPKQGS

SEQID No:155

MSIMSYNGGAVMAMKGKNCVAIAADRRFGIQAQMVTTDFQKIFPMGDRLYIGLAGLATD  
VQTVAQRLKFRLNLYELKEGRQIKPYTLMSMVANLLYEKRFPGPYTEPVIAGLDPKTFKP  
FICSLDLIGCPMVTDDFVVSGTCAEQMYGMCESLWEPNMDPDHLFETISQAMLNAVDR  
DAVSGMGVIVHIIKDKITTRTLKARM

SEQID No:156

MEAFGLSRGLWAGGPAPGQFYRIPSTPDSFMDPASALYRGPITRTQNPMVTGTSLVG  
VKFEGGVVIAADMLGSYGLARFRNISRIMRVNNSTMLGASGDYADFQYLKQVLGQMVI  
DEELLGDGHSYSPRAIHSWLTRAMYSRRSKMNPLWNTMVIGGYADGESFLGYVDMLG  
VAYEAPSLATGYGAYLAQPLLREVLEKQPVLSQTEARDLVERCMRVLYYRDARSYNRF  
QTATVTEKGVEIEGPLSTETNWDIAHMISGFE

SEQID No:157

MALASVLERPLPVNQRGFFGLGGRADLLDLGPGSLSDGLSLAAPGWGVPEEPGIEMLH  
GTTTLAFKFRHGVIVAADSRATAGAYIASQTVKKVIEINPYLLGTMAGGAADCSFWERLL  
ARQCRIYELRNKERISVAAASKLLANMVYQYKGMGLSMGMTMICGWDKRGPGLYYVDSE  
GNRISGATFSVGSGSVYAYGVMDRGYSYDLEVEQAYDLARRAIYQATYRDAYS GGAVN  
LYHVREDGWIRVSSDNVADLHEKYSGSTP

SEQID No:158

MAATLLAARGAGPAPAWGPEAFTPDWESREVSTGTTIMAVQFDGGVVLGADSRTTTG  
SYIANRVTDKLTPIHDRIFCCRS GSAADTQAVADAVTYQLGFHSLNEPPLVHTAASLFK  
EMCYRYREDLMAGIIAGWDPQEGGQVYSVPMGGMMVRQSFAGGSGSSYIYGYVDA  
TYREGMTKEECLQFTANALALAMERDGSSGGVIRLAAIAESGVERQVLLGDQIPKFAVA  
TLPPA

SEQID No:159

MGQSQSGGHGPGGGKKDDKDKKKKYEPPVPTRVGKKKKKTKGPDAASKLPLVTPHT  
 QCRLKLLKLERIKDYLLMEEEFIRNQEQMUPLEEKQEEERSKVDDLRGTPMSVGTLEEII  
 DDNHAIVSTSVGSEHYVSILSFVDKDLLEPGCSVLLNHKVHAVIGVLMDDTDPLVTVMKV  
 EKAPQETYADIGGLDNQIQEIKESVELPLTHPEYYEEMGIKPPKGVILYGPPGTGKTLLAK  
 AVANQTSATFLRVVGSELIQKYLGDGPKLVRELFRVAEEHAPSIVFIDEIDAIGTKRYDSN  
 SGGEREIQRTMLELLNQLDGFDSRGDVKVIMATNRIETLDPALIRPGRIDRKIEFPLPDEK  
 TKKRIFIHTSRMTLADDVTLLDLIMAKDDLSGADIKAICTEAGLMALRERRMKVTNEDF  
 KSKSENVLYKKQEGTPEGLYL

SEQID No:160

MPDYLGAQQRKTKEDKDDKPIRALDEGDIALLKTYGQSTYSRQIKQVEDDIQQLLKIN  
 ELTGIKESDTGLAPPALWDLAADKQTLQSEQPLQVARCTKIINADSEDPKYIINVKQFAKF  
 VVDLSQVAPTDIEEGMRVGVDRNKYQIHIPLPPKIDPTVTMMQVEEKPDVTYSVGGC  
 KEQIEKLREVVETPLLHPERFVNLGIEPPKGVLLFGPPGTGKTLCAVANRTDACFIRVI  
 GSELVQKYVGEGARMVRELFEMARTKKACLIFFDEIDAIGGARFDDGAGGDNEVQRTM  
 LELINQLDGFDPNGNIKVLNATNRPDTLDPALMRPGRDLDRKIEFSLPDLEGRTHIFKIHAR  
 SMSVERDIRFELLARLCPNSTGAEIRSVCTEAGMFAIRARRKATEKDFLEAVNKVIKSYA  
 KFSATPRYMTYN

SEQID No:161

MNLLPNIESPVTRQEKMATVWDEAEQDGIGEEVLKMSTEEIIQRTRLLDSEIKIMKSEVL  
 RVTHELQAMKDKIKENSEKIKVNKTLPYLVSNVIELLDVDPNDQEEDGANIDLDSQRKKGK  
 CAVIKTSTRQTYFLPVIGLVDAEKLKPGDLVGVNKSYSILETLPTHEYDSRVKAMEVDER  
 PTEQYSDIGGLDKQIQELVEAIVLPMNHKEKFENLGIQPPKGVLMYGPPGTGKTLLARAC  
 AAQTKATFLKLAGPQLVQMFIGDGAKLVRDAFALAKEKAPSIIFIDELDAIGTKRFDSEKA  
 GDREVQRTMLELLNQLDGFQPNQVQVIAATNRVDILDPALLRSGRLDRKIEFPMPNEE  
 ARARIMQIHSRKMNVSPPDVNYEELARCTDDFNGAQCKAVCVEAGMIALRRGATELTHE  
 DYMEGILEVQAKKANLQYYA

SEQID No:162

MEEIGILVEKAQDEIPALSVSRPQTGLSFLGPEPEDLEDLYSRYKKLQQELEFLEVQEEYI  
 KDEQKNLKKEFLHAQEEVKRIQSIPLVIGQFLEAVDQNTAIVGSTTGSNYYVRILSTIDRE  
 LLKPNASVALHKHSNALVDVLPPEADSSIMMLTSDQKPDVMIYADIGGMDIQKQEVREAV

ELPLTHFELYKQIGIDPPRGVLMYGPPGCGKTMLAKAVAHHTTAAFIRVVGSEFVQKYL  
 GEGPRMVRDVFRLAKENAPAIIFIDEIDAIATKRFDQAQTGADREVQRILLELLNQMDGFD  
 QNVNVKVIMATNRADTLDPALLRPGRRLDRKIEFPLPDRRQKRLIFSTITSKMNLSSEVDL  
 EDYVARPDKISGADINSICQESGMLAVRENRYIVLAKDFEKAYKTVIKKDEQEHEFYK

SEQID No:163

MALDGPEQMELEEGKAGSGLRQYYLSKIEELQLIVNDKSQNLRRRLQAQRNELNAKVRL  
 REELQLLQEQGSYVGEVVRAMDKKKVLVKVHPEGKFVVDVDKNIDINDVTPNCRVALR  
 NDSYTLHKILPNKVDPLVSLMMVEKVPDSTYEMIGGLDKQIKEIKEVIELPVKHPELFEAL  
 GIAQPKGVLVLYGPPGTGKTLLARAVAHHTDCTFIRVSGSELVQKFIGEGARMVRELFVM  
 AREHAPSIIFMDEIDSIGSSRLEGGSGGDSEVQRTMLELLNQLDGFEATKNIKVIMATNRI  
 DILDSALLRPGRIDRKIEFPPPNEEARLDILKIHSRKMNLTRGINLRKIAELMPGASGAEVK  
 GVCTEAGMYALRERRVHVTQEDFEMAVAKVMQKDSEKNMSIKKLWK

SEQID No:164

MADPRDKALQDYRKLLLEHKEIDGRLKELREQLKELTKQYEKSENDLKALQSVGQIVGE  
 VLKQLTEEFKIVKATNGPRYVVGCRRLDKSKLKPGRTRVALDMTTLTIMRYLPREVDPL  
 VYNMSHEDPGNVSYSEIGGLSEQIRELREVIELPLTNPELFQRVGIIPPKGCLLYGPPGT  
 GKTLLARAVASQLDCNFLKVVSSSIVDKYIGESARLIREMFNYARDHQPCIIFMDEIDAIG  
 GRRFSEGTSADREIQRTLMELLNQMDGFDTLHRVKMIMATNRPDTLDPALLRPGRRLDR  
 KIHIDLPNEQARLDILKIHAGPITKHGEIDYEAIVKLSDGFNAGADLRNVCTEAGMFAIRADH  
 DFVVQEDFMKAVRKVADSKKLESKLDYKPV

SEQID No:165

MITSAAGIISLLDEDEPQLKEFALHKLNAVVNDFWAEISESVDKIEVLYEDEGFRSRQFAA  
 LVASKVFYHLGAFFEESLNYALGARDLFNVNDNSEYVETIIAKCIDHYTKQCVENADLPEG  
 EKKPIDQRLEGIVNKMFRCLDDHKYKQAIGIALETRRLDVFEKTILESNDVPGMLAYSL  
 KLCMSLMQNKQFRNKVLRVLVKIYMNLEKPDFINVCQCLIFLDDPQAVSDILEKLVKEDN  
 LLMAYQICFDLYESASQQFLSSVIQNLRTVGTPIASVPGSTNTGTVPGSEKSDSDSMETE  
 EKTSSAFVGKTPEASPEPKDQTLKMIKILSGEMAIELHLQFLIRNNNTDLMILKNTKDAVR  
 NSVCHTATVIANSFMHCGTTSQFLRDNLEWLARATNWAKFTATASLGVHKGHEKEAL  
 QLMATYLPKDTSPGSAYQEGGGLYALGLIHANHGDIIDYLLNQLKNASNDIVRHGGSL  
 GLGLAAMGTARQDVYDLLKTNLYQDDAVTGEAAGLALGLVMLGSKNAQAIEDMVGAYAQ  
 ETQHEKILRGLAVGIALVMYGRMEEADALIESLCRDKDPILRRSGMYTVAMAYCGSGNN

KAIRRLHVAVSDVNDDVRSAAVESLGFILFRTPEQCPSVVSLLSESYNPHVRYGAAMA  
 LGICCAGTGNKEAINLLEPMTNDPVNYVRQGALIASALIMIQQTEITCPKVNQFRQLYSKV  
 INDKHDDVMAKFGAILAQGILDAGGHNVITISLQSRTGHTHMPSVVGVLVFTQFWFWFPL  
 SHFLSLAYTPTCVIGLNKDLKMPKVQYKSNCKPSTFAYPAPLEVPEKEKEKEKVSTAVLSI  
 TAKAKKKEKEKEKEKEEKEMEVDEAEKKEEKEKKKEPEPNFQLLDNPARVMMPAQLKVLT  
 MPETCRYQPFKPLSIGGIILKDTSEDIEELVEPVAAHGPKEIEEEEQEPEPPEPFEYIDD

SEQID No:166

MAAAAVVEFQRAQSLLSTDREASIDILHSIVKRDIEENDEEAVQVKEQSILELGSLLAKTG  
 QAAELGGLLKYYVRPFLNSISKAKAARLVRSLLDLFLDMEAATGQEVELCLECIEWAKSEK  
 RTFLRQALEARLVSLYFDTKRYQEALHLGSQLLRELKKMDDKALLVEVQLLESKTYHAL  
 SNLPKARAALTSARTTANAIYCPPKLQATLDMQSGIIHAAEEKDWKTAYSIFYEAFEGYD  
 SIDSPKAITSCLKYMLLCKIMLNTPEDVQALVSGKLALRYAGRQTEALKCVAQASKNRS  
 LA DFEKALTDYRAELRDDPIISTHLAKLYDNLLEQNLIRVIEPFSRVQIEHISSLIKLSKADVER  
 KLSQMILDKKFHGLDQGEVLIIFDEPPVDKTYEAALETIQNMSKVVDLSLYNKAKKLT

SEQID No:167

MADGGSERADGRIVKMEVDYSATVDQRLPECAKLAKEGRLQEVIETLLSLEKQTRTASD  
 MVSTSRILVAVVKMCYEAKEDWLLNENIMLLSKRRSQLKQAVAKMVQQCCTYVEEITDL  
 PIKRLIDTLRMVTEGKIYVEIERARLTKTLATIKEQNGDVKEAASILQELQVETYGSMEKK  
 ERVEFILEQMRLCLAVKDYIRTQIISKINTKFFQEENTEKLKLKYNNLMIQLDQHEGSYLS  
 ICKHYRAIYDTPCIQAESEKWQQALKSVVLYVILAPFDNEQSDLVHRISGDKKLEEIPKYK  
 DLLKLFTTMELMRWSTLVEDYGMELRKGSLESPATDVFGSTEEGEKRWKDLKNRVVE  
 HNIRIMAKYYTRITMKRMAQLLDLSVDESEAFSLNLVVNKTIFAKVDRLAGIINFQRPKDP  
 NNLLNDWSQKLNSLMSLVNKTTHLIAKEEMIHNLQ

SEQID No:168

MKDVPGLQSQNSGPGQPAVWHRLEELYTKKLWHQLTLQVLDFVQDPCFAQGDGLI  
 KLYENFISEFEHRVNPLSLVEIILHVVRQMTDPNVALTFLEKTREKVKSSDEAVILCKTAIG  
 ALKLNIGDLQVTKETIEDVEEMLNNLPGVTSVHSRFDLSSKYYQTIGNHASYYKDARF  
 LGCVDIKDLPVSEQQERAFTLGLAGLLGEGVFNFGEMLMHPVLESRLNTDRQWLIDTLY  
 AFNSGNVERFQTLKTAWGQQPDLAANEAQLLRKIQLLCLMEMTFTRPANHRQLTFEEIA  
 KSAKITVNEVELLMKALSVGLVKGSIDEVDKRVHMTWVQPRVLDLQQIKGMKDRLEF  
 WCTDVKSMEMLVEHQAHDILT

SEQID No:169

MEEGGRDKAPVQPQQSPAAAPGGTDEKPSGKERRDAGDKDKEQELSEEDKQLQDEL  
 EMLVERLGEKDTSLYRPALEELRRQIRSSTTSMTSVPKPLKFLRPHYGKLKEIYENMAP  
 GENKRFAADIISVLAMTMSGERECLKYRLVGSQEELASWGHEYVRHLAGEVAKEWQEL  
 DDAEKVQREPLTLVKEIVPYNMAHNAEHEACDLLMEIEQVDMLEKDIDENAYAKVCLYL  
 TSCVNYVPEPENSALLRCALGVFRKFSRFPALRLALMLNDMELVEDIFTSCKD VVVQK  
 QMAFMLGRHGVFLELSEDVEEYEDLTEIMSNVQLNSNFLALARELDIMEPKVPDDIYKT  
 HLENNRFGGSGSQVDSARMNLASSFVNGFVNAAFQGDKLLTDDGNKWLYKNKDHGM  
 LSAAASLGMILLWDVDGGLTQIDKYLYSSEDIKSGALLACGIVNSGVRNECDPALALLS  
 DYVLHNSNTMRLGSIFGLGLAYAGSNREDVLTLLLPVMGDSKSSMEVAGVTALACGMIA  
 VGSCNGDVTSTILQTIMEKSETELKDTYARWLPLGLGLNHLGKGEAIEAILAALEV VSEPF  
 RSFANTLV DVCAYAGSGNV LKVQQLLHCSEHFDSKEKEEDKDKKEKKDKDKKEAPAD  
 MGAHQGVAVLGIALIAMGEEIGAEMALRTFGHLLRYGEPTLRRAVPLALALISVSNPR LNI  
 LDTLSKFSDADPEVSYN SIFAMGMVGS GTNNARLAAML RQLAQYHAKDPNNLFMVRL  
 AQGLTHLGKGTLTLC PYHSDRQLMSQVAVAGLLTVLVSF LDVRNIILGKSHYVLYGLVAA  
 MQPRMLVTFDEELRPLPVSVRVGQAVDVVGQAGKPKTITGFQTH TTPVLLAHGERAEL  
 ATEEF LPTPILEGFVILRKPNPNYDL

SEQID No:170

MKQEGSARRRGADKAKPPPGGGEQEPPPPAPQDVEMKEEAATGGGSTGEADGKTA  
 AAAAEHSQRELD T V TLEDIKEHV KQLEKAVSGKEPRFVLRALRMLPSTSRRLNHVLYK  
 AVQGFFTSNNATRD FLLPFLE EPM DTEADLQFRPRTGKAASTPLLPEVEAYLQLLVIFM  
 MNSKRYKEAQKISDDL MQKISTQNRRALDLVAAKCYYYHARVYEF LDKLDVVR SFLHAR  
 LRTATLRHDADGQATLLN LLLRNYLHYS LYDQAEKLVSKSVFPEQANNNEWARYLYYT  
 GRIKAIQLEYSEARRTMTNALRKAPQHTAVGFKQTVHKLLIVVELLLGEIPDRLQFRQPSL  
 KRSLMPYFLLTQAVRTGNLAKFNQVLDQFGEKFQADGTYTLIIRLRHNVIKTGVRMISLS  
 YSRISLADIAQKLQLD SPEDA EFIVAKAIRDGVIEASINHEKGYVQSKEMIDIYSTREPQLA  
 FHQRISFC LDIHNMSV KAMRFPPKSYN KDLES AEEERREREQQDLEFAKEMAEDDDDSF  
 P

SEQID No:171

MVLESTMVCVDNSEYMRNGDFLPTRLQAQQDAVNIVCHSKTRSNPENNVGLITLANDC  
 EVLTTLTPTDGRILSKLHTVQPKGKITFCTGIRVAHLALKHRQGKNHKMR IIAFVGSPVED

NEKDLVKLAKRLKKEKVNVDIINFGEEEVNTEKLTAFVNTLNGKDGTGSHLVTVPGPSL  
 ADALISSPILAGEGGAMLGLGASDFEFGVDPSADPELALALRVSMEEQRQRQEEEEARR  
 AAAASAAEAGIATTGTEDSDDALLKMTISQQEFGRTGLPDLSSMTEEEQIAYAMQMSLQ  
 GAIEFGQAESADIDASSAMDTSEPAKEEDDYDVMQDPEFLQSVLENLPGVDPNNEAIRN  
 AMGSLASQATKDGKKDKKKEEDKK

SEQID No:172

MLTFMASDSEEEVCDERTSLMSAESPTPRSCQEGRQGPEDGENTAQWRSQENEEDG  
 EEDPDRYVCSGVPGRPGLLEEELTKYGAKHVIMLFVPVTLCMIVVATIKSVRFYTEKN  
 GQLIYTPFTEDTPSVGQRLNLSVLNLTLMISVIVVMTIFLVVLYKYRCYKFIHGWLIMSSLM  
 LLFLFTYIYLGEVLKTYNVAMDYPTLLLTVWNFGAVGMVCIHWKGPLVLQQAYLIMISAL  
 MALVFIKYLPEWSAWVILGAISVYDLVAVLCPKGPLRMLVETAQERNEPIFPALYSSAMV  
 WTVGMAKLDPSSQGALQLPYDPEMEEDSYDSFGEPSYPEVFEPPLTGYPGEELEEEE  
 ERGVKLGLGDFIFYSVLVGKAAATGSGDWNTTLACFVAILIGLCLTLLLAVFKKALPALPI  
 SITFGLIFYFSTDNLVRPFMDTLASHQLYI

SEQID No:173

MAAKVFESIGKFGLALAVAGGVVNSALYNVDAGHRAVIFDRFRGVQDIVVGEGTHFLIP  
 WVQKPIIFDCRSRPRNPVITGSKDLQNVNITLRLFRPVASQLPRIFTSIGEDYDERVLPS  
 ITTEILKSVVARFDAGELITQRELVSQVSDDLTERAATFGLILDDVSLTHLTFGKEFTEAV  
 EAKQVAQQEAERARFVVEKAEQQKAAIISAEGDSKAAELIANSLATAGDGLIELRKLEA  
 AEDIAYQLSRSRNITYLPAGQSVLLQLPQ

SEQID No:174

MPLAQLADPWQKMAVESPSDSAENGQQIMDEPMGEEEEINPQTEEVSIKEIAITHHVKEG  
 HEKADPSQFELLKVLGQGSFGKVFLVKKISGSDARQLYAMKVLKKATLKVRDRVRTKM  
 ERDILVEVNHPFIVKLHYAFQTEGKLYLILDFLRGGDLFTRLKSKEVMFTEEDVKFYLAELA  
 LALDHLHSLGIIYRDLKPENILLDEEGHIKLTDFGLSKESIDHEKKAYSFCGTVEYMAPEV  
 VNRRGHTQSADWWSFGVLMFEMLTGTLPFQKGDRKETMTMILKAKLGMPQFLSPEAQ  
 SLLRMLFKRNPANRLGAGPDGVEEIKRHSFFSTIDWNKLYRREIHPPFKPATGRPEDTF  
 YFDPEFTAKTPKDSPGIPPSANAHQLFRGFSFVAITSDDSQAMQTVGVHSIVQQLHRN  
 SIQFTDGYEVKEDIGVGSYSVCKRCIHKATNMEFAVKIIDKSKRDPTEEIEILLRYGQHPNI  
 ITLKDVYDDGKYVYVVTLMKGGELLDKILRQKFFSEREASAVLFTITKTVEYLHAQGVV  
 HRDLKPSNILYVDESGNPESIRICDFGFAKQLRAENGLLMTPCYTANFVAPEVLKRQGY

DAACDIWSLGVLLYTMLTGYTPFANGPDDTPEEILARIGSGKFSLSGGYWNSVSDTAKD  
 LVSKMLHVDPHQRLTAALVLRHPWIVHWDQLPQYQLNRQDAPHLVKGAMAATYSALN  
 RNQSPVLEPVGRSTLAQRRGIKKITSTAL

SEQID No:175

SVTQPAGSVMGRWSLTASPVTLTSLLPMVTAGPAAGKSSSSTSWDTVLTAITCASTVQ  
 LISTTLGASASGARMPPTCCSGTTVFLTALQDTMQREELVKNATPPAEPARAEDLSPAP  
 HVTPTSCCPTLAPAAPPASLGTILMTIMFASTQSQWSIEVGVDDHFLDLQQKTSLFKKV  
 WPHQDVCVSTTCNTHCGSCDSQASCTSCRDPNKVLLFGECQYESCAPQYYLDFSTNT  
 CKAADRVLINELLGLRVDRKEDNLMQTTFFLECDWSCSACSGPLKTDCLQCMDGYVLQD  
 GACVEQCLSSFYQDSGLCKNCDSYCLQCQGPHECTRCKGPFLLLEAQCVQECGKGYF  
 ADHAKHKCTACPQGCLQCXHRDRCHLCDHGFFLKSGLCVYNVCVPGFSVHTSNETCSG  
 KIHTPSLHVNGSLILPIGSIKPLDFSLLNVQDQEGRVEDLLFHVVSTPTNGQLVLSRNGKE  
 VQLDKAGRFSWKDVNEKKVRFVHSKEKLRKGYLFLKISDQQFFSEPQLINIQAFSTQAP  
 YVLRNEVLHISRGERATITTQMLDIRDDDNPDQDVVIEIIDPPLHGQLLQTLQSPATPIYQF  
 QLDELSRGLLHYAHDGSDSTSDVAVLQANDGHSFHNILFQVKTVPNDRGLQLVANS  
 VWVPEGGMLQITNRILQAEAPGASAEIYKITQDYPQFGEVVLLVNMPADSPADEGQH  
 LPDGRTATPTSTFTQQDINEGIVWYRHSGAPAQSDSFRFEVSSASNAQTRLESHMFNIA  
 ILPQTPEAPKVSLEASLHMTAREDGLTVIQPHSLSFINSEKPSGKIVYNITLPLHPNQGIIE  
 HRDHPHSPIRYFTQEDINQGKVMYRPPPAAPHLQELMAFSFA

SEQID No:176

MSSQPAGNQTSPGATEDYSYGSWYIDEPQGGEELQPEGEVPSCHTSIPPGLYHACLA  
 SLSILVLLLLAMLVRRRQLWPDCVRGRPLPSPVDFLAGDRPRAVPAAVFMVLLSSLCL  
 LLPDEDALPFLTASAPSQDGKTEAPRGAWKILGLFYAALYYPLAACATAGHTAAHLLG  
 STLSWAHLGVQVWQRAECPQVPKIYKYSSLLASLPLLLGLGFLSLWYPVQLVRSFSRRT  
 GAGSKGLQSSYSEEYLRNLLCRKKLGSSYHTSKHGFLSWARVCLRHCIYTPQPGFHL  
 LKLVLSATLTGTAIYQVALLLVGVVPTIQKVRAGVTTDVSYLLASFGIVLSEDKQEVELV  
 KHHLWALEVCYISALVLSCLLTFVLMSLVTHRTNLRALHRGAALDLSPLHRSPHPSRQ  
 AIFCWMSFSAYQTAFICLGLLVQQIIFLGTTALAFLVLMPLVHGRNLLLFRSLESSWPFW  
 LTLALAVILQNMAAHWVFLETHDGHPQLTNRRVLYAATFLLFPLNVLVGAMVATWRVLL  
 SALYNAILGQMDLSLLPPRAATLDPGYTYRNFLKIEVSQSHPAMTAFCSLLLQAQSL  
 PRTMAAPQDSLPGEEDEGMQLLQTKDSMAKGARPGASRGRARWGLAYTLLHNPTL  
 QVFRKTALLGANGAQP



SEQID No:177

MERPWGAADGLSRWPHGLGLLLLLLQLLPPSTLSQDRLDAPPPPAAPLPRWSGPIGVS  
WGLRAAAAGGAFFRGGRRWSAPGEDEECGRVRDFVAKLANNTHQHVFDDLGRGSVS  
LSWVG DSTGVILVLTTFHVPLVIMTFGQSKLYRSEDYGKNFKDITDLINNTFIRTEFGMAI  
GPENSGKVVLTAEVSGGSRGGRIFRSSDFAKNFVQTDLPFHPLTQMMYSPQNSDYLLA  
LSTENGLWVSKNFGGKWEEIHKAVCLAKWGS DNTIFFTTYANGSCKADLGALELWRTS  
DLGKSFKTIGVKIYSFGLGGRFLFASVMADKDTTRRIHVSTDQGD TWSMAQLPSVGQE  
QFYSILAANDDMVFMHVDEPGDTGFGTIFTSDDRGIVYSKSLDRHLYTTTGGETDFTNV  
TSLRGVYITSVLSEDNSIQTMITFDQGGRWTHLRKPENSECDATAKNKNECSLHIHASY  
SISQKLNVPMAPLSEPNAVGI VIAHGSVGD AISVMVPDVYISDDGGYSWTKMLEGPHY  
TILDSGGIIVAEIHSSRPINVIKFSTDEGQCWQTYTFTRDPIYFTGLASEPGARSMNISIWG  
FTESFLT SQWVSYTIDFKDILERNCEEKDYTIWLAHSTD PEDYEDGCILGYKEQFLRLRK  
SSMCQNGRDYVVT KQPSICLCSLEDFLCDFGYR PENDSKCVEQPELKGHDLEFCLYG  
REEHLTTNGYRKIPGDKCQGGVNPVREV KDLKKKCTSNFLSPEKQNSKSN SVPIILAIVG  
LMLVT VVAGVLIVKKYVCGGRFLVHRYSVLQQHAEANGVDGVDALDTASHTNKSGYHD  
DSDEDLLE

SEQID No:178

MPAHL LQDDISSSYTTTTTITAPPSRVLQNGGDKLETMPLYLEDDIRPDIKDDIYDPTYKD  
KEGPSPKVEYVWRNIILMSLLHLGALYGITLIPTCKFYTWLWGVFYFVSALGITAGAHRL  
WSHRSYKARLPLRLFLIIANTMAFQNDVYEW ARDHRAHHKFSETHADPHNSRRGFFFS  
HVGWLLVRKHPAVKEKGSTLDLSDEAEKLV MFQRRYYKPGLLMMCFILPTLV PWYFW  
GETFQNSVFVATFLRYAVVLNATWL VNSAAHLFGYR PYDKNISPRENILVSLGAVGEGF  
HNYHHSFPYDYSASEYRWHINFTTFFIDCMAALGLAYDRKKVSKAAILARIKRTGDGNYK  
SG

SEQID No:179

MAAAAPGN GRASAPRLLLLFLVPLLWAPAAVRAGPDEDLSHRNKEPPAPAQQQLQPQPV  
AVQGPEPARVEKIFT PAAPVHTNKEDPATQTNLGFIHAFVAAISVIIVSELGDKTFFIAAIM  
AMRYNRLTVLAGAMLALGLMTCLSVLFGYATTVIPRVYTYVSTVLFAIFGIRMLREGLK  
MSPDEGQEELEEVQAE LKKKDEEFQRTKLLNGPGDVETGTSITVPQKKWLHFISPIFVQ  
ALTLTFLAEWGDRSQLTTIVLAAREDPYGVAVGGTVGHCLCTGLAVIGGRMIAQKISVRT  
VTIIGGIVFLAFAFSALFISPD SGF

SEQID No:180

MTSIHFVVHPLPGTEDQLNDRLREVSEKLNKYNLNSHPPLNVLEQATIKQCVVGPNHAA  
 FLLEDGRVCRIGFSVQPDRLELGKPDNNDGSKLNSNSGAGRTSRPGRTSDSPWFLSG  
 SETLGRLAGNTLGSRWSSGVGGSSGGSSGRSSAGARDSRRQTRVIRTGRDRGSGLL  
 GSQPQPVIPASVIPEELISQAQVVLQGKSRSVIIRELQRTNLDVNLAVNNLLSRDDEDGD  
 DGDDTASESYLPGEDLMSLLDADIHSAHPSVIIDADAMFSEDISYFGYPSFRRSSLSRLG  
 SSRVLLLPLERDSELLRERESVLRLRERRWLDGASFDNERGSTSKEGEPNLDKKNTPV  
 QSPVSLGEDLQWWPDKDGTKFICIGALYSELLAVSSKGELYQWKWSESEPYRNAQNP  
 SLHHPRATFLGLTNEKIVLLSANSIRATVATENNKVATWVDETLSSVASKLEHTAQTYSE  
 LQGERIVSLHCCALYTCAQLENSLYWWGVVPPFSQRKKMLEKARAKNKKPKSSAGISSM  
 PNITVGTQVCLRNPLYHAGAVAFSISAGIPKVGVLMEVWNMNDSCRFLRSPESLKN  
 MEKASKTTEAKPESKQEPVKTEMGPPSPASTCSDASSIASSASMPYKRRRSTPAPKE  
 EEKVNEEQWSLREVVFVEDVKNVPVGKVLKVDGAYVAVKFPGTSSNTNCQNSSGPDA  
 DPSSLLQDCRLLRIDELQVVKTTGGTPKVPDCFQRTPKKLCIPEKTEILAVNVDSKGVHAV  
 LKTGNWVRYCIFDLATGKAEQENNFPTSSIAFLGQNERNVAIFTAGQESPIILRDGNGTIY  
 PMAKDCMGGIRDPDWLDLPPISSLGMGVHSLINLPANSTIKKKAAVIIMAVEKQTLMQHIL  
 RCDYEACRQYLMNLEQAVVLEQNLQMLQTFISHRCDGNRNHLHACVSVCFPTSNKETK  
 EEEEEAERSERNTFAERLSAVEAIAANAISVVSSNGPGNRAGSSSSSRSLRLREMMRRSLR  
 AAGLGRHEAGASSSDHQDPVSPPIAPPSWVPDPPAMDPDGDIDFILAPAVGSLTTAATG  
 TGQGPSTSTIPGPSTEPSVVESKDRKANAHFILKLLCDSVVLQPYLRELLSAKDARGMT  
 PFMSAVSGRAYPAAITILETAQKIAKAEISSSEKEEDVFMGMVCPSGTNPDDSPLYVLCC  
 NDTCSFTWTGAEHINQDIFECRTCGLLESLLCCCTECARVCHKGHDCCLKRTSPTAYCD  
 CWEKCKCKTLIAGQKSARLDLLYRLLTATNLVTLPNRGEHLLLFLVQTVARQTVEHCQ  
 YRPPRIREDNRNKTASPEDSDMPDHDLEPPRFAQLALERVLDWNALKSMIMFGSQEN  
 KDPLSASSRIGHLLPEEQVYLNQQSGTIRLDCFTHCLIVKCTADILLDDTLGTLVKELQN  
 KYTPGRREEAIAVTMRFLRSVARVVFILSVEMASSKKKNNFIPQPIGKCKRVFQALLPYA  
 VEELCNVAESLIVPVRMGIARPTAPFTLASTSIDAMQGSEELFSVEPLPPRPSSDQSSSS  
SQSQSSYIIRNPQQRRIQSQPVRGRDEEQDDIVSADVEEVEVVEGVAGEEDHHDEQE  
 EHGEENAEAEQGQHDEHDEDGSDMELDLLAAETESDSESNHSNQDNASGRRSVVTAA  
 TAGSEAGASSVPAFFSEDDQSNDSSSDSSSSSQSDDIEQETFMLDEPLERTTNSSHA  
 NGAAQAPRSMQWAVRNTQHQRRAASTAPSSTSTPAASSAGLIYIDPSNLRRTISTSA  
 AAAAALASNASSYLTSASSLARAYSIVIRQISDLMLIPKYNHLVYSQIPAAVKLTYQDA  
 VNLQNYVEEKLIPTWNWMVSIMDSTEALRYGSALASAGDPGHPNHPLHASQNSARR

ERMTAREEASLRTLEGRRRATLLSARQGMMSARGDFLNYALSLMRSHNDEHSDVLPV  
 LDVCSLKHVAYVFQALIYWIKAMNQTTLDTPQLERKRTRELLELGIDNEDSEHENDDD  
 TNQSATLNDKDDDSLPAETGQNHPFFRRSDSMTFLGCIPPNPFEVPLAEAIPLADQPHL  
 LQPNARKEDLFGRRPSQGLYSSSASSGKCLMEVTVDRNCLEVLPTKMSYAANLKNVMN  
 MQNRQKKEGEEQPVLPEETESSKPGPSAHDLAACLKSSLLAEIGLTESEGPPLTSFRPQ  
 CSFMGMVISHDMLLGRWRLSLELFGRVFMEDVGAEPGSILTELGGFEVKESKFRREME  
 KLRNQQSRDLSLEVDRDRDRLLIQQTMRQLNNHFGRRCATTPMAVHRVKVTFKDEPGE  
 GSGVARSFYTAIAQAFLSNEKLPNLECIQNANKGTHTSMLQRLNRNGERDRERERERE  
 MRRSSGLRAGSRRDRDRDFRRQLSIDTRPFRPASEGNPSDDPEPLPAHRQALGERLY  
 PRVQAMQPAFASKITGMILLESPAQLLLLLLASEDSLRRARVDEAMELIIAHGRENGADSIL  
 DLGLVDSSEKVQQENRKRHGSSRSVVDMDLDDTDDGDDNAPLFYQPGKRGFYTPRP  
 GKNTearLNCFRNIGRILGLCLLQNELCPITLNRHVIVKLLGRKVNWHDFAFFDPVMYES  
 LRQLILASQSSDADAVFSAMDLAFAIDLCKEEGGGQVELIPNGVNIPVTPQNVYEVVRKY  
 AEHRMLVVAEQPLHAMRKGLLDVLPKNSLEDLTAEDFRLLVNGCGEVNVQMLISFTSFN  
 DESGENAEKLLQFKRWFWSIVEKMSMTERQDLVYFWTSSPSLPASEEGFQPMPSITIR  
 PPDDQHLPTANTCISRLYVPLYSSKQILKQKLLLAIKTKNFGFV

SEQID No:181

MATHGQTCARPMCIPPSYADLGKVARDIFNKGFGFGLVKLDVKTSCSGVEFSTSGSS  
 NTDTGKVTGTLETYKWCEYGLTFTEKWNTDNTLGTEIAIEDQICQGLKLTFTDFTSPNT  
 GKKSGBKIKSSYKRECINLGCDVDFDFAGPAIHGSAVFGYEGWLAGYQMTFDSAKSKLT  
 RNNFAVGYRTGDFQLHTNVNDGTEFGGSIYQKVCEDLDTSVNLAWTSGTNCTRFGIAA  
 KYQLDPTASISAKVNNSSLIGVGYTQTLRPGVKLTLSALVDGKSINAGGHKVGLELEA

SEQID No:182

MDSNTAPLGPSCPQPPAPQPQARSRLNATASLEQERSERPRAPGPQAGPGPGVRD  
 AAAPAEPPAQHTRSRRERADGTGPTKGDMEIPFEEVLERAKAGDPKAQTEVGKHYLQLA  
 GDTDEELNSCTAVDWLVLAQKQGRREAVKLLRRCLADRRGITSENEREVRQLSSETDL  
 ERAVRKAALVMYWKLNPKKKKQVAVAELENVGVNEHDGGAQPGVPKSLQKQRR  
 MLERLVSSSESKNYIALDDFVEITKKYAKGVIPSSLFLQDDEDDDELAGKSPEDLPLRLKV  
 VKYPLHAIMEIKEYLIDMASRAGMHWLSTIIPTHHINALIFFFIISNLTIDFFAFFIPLVIFYLSF  
 ISMVICTLKVFQDSKAWENFRTLTDLLLRFEPNLDVEQAEVNFGWNHLEPYAHFLLSVFF  
 VIFSFPISKDCIPCSELAVITGFFTTSYLSLSTHAEPYTRRALATEVTAGLLSLLPSMPL  
 NWPYLVKVLGQTFITVPVGHLLVNLVSVPCLLYVYLLYLFFRMAQLRNFKGTICYLVPYLV

CFMWCELSVVILLESTGLGLLRASIGYFLFLFALPILVAGLALVGVLQFARWFTSLELTkia  
 VTVAVCSVPLLLRWWTkasFSVVGmVksLTrSSmVKLILVWLTAIVLFCWFYVYRSEGm  
 KVYNSTLTWQQYGALCGPRAWKETNMARTQILCSHLEGHRVTWTGRFKYVRVTDIDN  
 SAESAINMLPFFIGDWMRCLYGEAYPACSPGNTSTAEELCRLKLLAKHPCHIKKFDRY  
 KFEITVGMPFSSGADGSRsREEDDVTKDIVLRASSEFKSVLLSLRQGSLEFSTILEGRlg  
 SKWPVFELKAISCLNCMAQLSPTRRHVKIEHDWRSTVHGAVKFAFDFFFFPFLSAA

SEQID No:183

MGSGPLSLPLALSPPRLLLLLLLLSLLPVARASEAEHRLFERLFEDYNEIRPVANVSDPVII  
 HFEVSMSQLVKVDEVNQIMETNLWLKQIWNDYKLKWNPSDYGGAEFMRVPAQKIWKp  
 DIVLYNNAVGDfQVDDKTKALLKYtGEVTWIPPAIFKSSCKIDVTYFPFDYQNCTMKFGS  
 WSYDKAKIDLVLIGSSMNLKDYWESGEWAIIKAPGYKHDIKYNCCeeIYPDITYSLYIRRL  
 PLFYtINLIIPCLLISFLTVLVFYLPsDCGEKVTLCISVLLSLTVFLLVITETIPSTSLVIPLIGEY  
 LLFTMIFVTLsIVITVFVLNVHYRTPtTHTMPSWVKTVFLNLLPRVMFMTRPTSNEGNAQ  
 KPRPLYGAELSNLNCFSRAESKGCKEGYPCQDGMCGYCHHRIKISNFSANLTrSSSS  
 ESVDaVLSLSALSPEIKEAIQSVKYIAENMKAQNEAKEEQKAQEIQQLKRKEKSTETSDQ  
 EPGL

SEQID No:184

MEKRETFVQAVSKELVGEFLQFVQLDKEASDPFSLNELLDELSRKQKEELWQRLKNLLT  
 DVLLESPVDGWQVVEAQGEDNMETEhGSKMRKSIEIIYAITSVILASVSVINESENYEALL  
 ECvIILNGILYALPESERKLQSSIQDLCVTWWEKGLPAKEDTGKtAFVMLLRRSLETKTG  
 ADVcRLWRIHQALYCFDYDLEESGEIKDMLLECfININyIKKEEGRRFLSCLFNWNINFIK  
 MIHGtIKNQLQGLQKSLMVYIAEIYfRAWKKASGKILEAIENDCIQDFMFHGIHLPRRSPV  
 HSKVREVLSYfHHQKKVRQGVEEMLYRlyKPILWRGLKARNSEVRsNAALLFVEAFPIR  
 DPNLHAIEMDSEIQKQFEELYSLLEDpYPMVRSTGILGVCKITSKYWEMMPPTILIDLLKK  
 VTGELAFDTSSADVRCsVFKCLPMILDNKLSHPLLEQLLPALRYSLHDNSEKVRVAFVD  
 MLLKIKAVRAAKFWKICPMEHILVRLETDSRPVSRRLVSLIFNSFLPVNQPEEVCERCv  
 TLVQMNHAAARRFYQYAHEHTACTNIAKLIHVIRHCLNACIQRAVREPPEDeEEEEEDGRE  
 KENVTVLDKTLsVNDVACMAGLLEIIVILWKSIDRSMENNKEAKLYTINKFASVLPEYLKV  
 FKDDRCKIPLFMLMSFMPASAVPPFSCGVISTLRSREEGAVDKSYCTLLDCLCSWGQV  
 GHILELVDNWLPTeHAQAKSNTASKGRVQIHdTRPVKPELALVYIEYLLThPKNRECLLS  
 APRKKLNHLLKALETskADLESLLQTPGGKPRGFSEAAAPRAfGLHCRLSIHLQHkFCS  
 EGKVYLSMLEDTGFWLESKILSFIQDQEEDYLKLHRVIYQQIIQTYLTVCKDVVMVGLGD

HQFQMQLLQSRSLGIMQTVKGFFYVSLLLDILKEITGSSLIQKTDSDDEEVAMLLDTVQKVF  
QKMLECIARSFRKQPEEGLRLLYSVQRPLHEFITAVQSRHTDTPVHRGVLSTLIAGPVVE  
ISHQLRKVSDVEELTPPEHLSDLPPFSRCLIGIIKSSNVVRSFLDELKACVASNDIEGIVCL  
TAAVHIILVINAGKHKSSKVREVAATVHRKLKTFMEITLEEDSIERFLYESSSRTL GELLNS

SEQID No:185

MAAAAVQGGRSGGSGGCSGAGGASNCGTGSGRSGLLDKWKIDDKPVKIDKWDGSAV  
KNSLDDSAKKVLEKYKYVENFGLIDGRLTICTISCFFAIVALIWDYMHFPFESKPVLALC  
VISYFVMMGILTIYTSYKEKSIFLVAHRKDPTGMDPDDIWQLSSSLKRFDCKYTLKLT F IS  
GRTKQQREAEFTKSIKFFDHSGTLVMDAYEPEISRLHDSLAIERKIK

SEQID No:186

MAVLRQLALLLWKNYTLQKRKVLVTVLELFLPLLFPGILIWLRLKIQSENVPNATIYPGQSI  
QELPLFFTFPPPGDTWELAYIPSHSDAAKTVTETVRRALVINMRVRGFPSEKDFEDYIRY  
DNCSSSVLAADVFEHPFNHSKEPLPLAVKYHLRFSYTRRNYMWTQTGSFFLKETEGWH  
TTSFLPLFPNPGPRELTSPDGGEPGYIREGFLAVQHAVDRAIMEYHADAATRQLFQRLT  
VTIKRFPYPPIADPFLVAIQYQLPLLLLLSFTYTALTARAVVQEKERRLKEYMRMMGLS  
SWLHWSAWFLLFFLFLIAASFMTLLFCVKVKPNVAVLSRSDPSLVLAFLLCFAISTISFSF  
MVSTFFSKANMAAAFSGGFLYFFTYIPYFFVAPRYNWMTLSQKLCSCLLSNVAMAMGAQ  
LIGKFEAKGMGIQWRDLLSPVNVDDDFCFGQVLGMLLLDSVLYGLVTWYMEAVFPGQF  
GVPQPWYFFIMPSYWCGKPRAVAGKEEEDSDPEKALRNEYFEAPEDLVAGIKIKHLSK  
VFRVGNKDRAAVRDLNLYEGQITVLLGHNGAGKTTTLSMLTGLFPPTSGRAYISGYEI  
SQDMVQIRKSLGLCPQHDILFDNLTVAEHLFYAQLKGLSRQKCPEEVKQMLHIIGLEDK  
WNSRSRFLSGGMRRKLSIGIALIAGSKVLILDEPTSGMDAISRRAIWDLLQRQKSDRTIVL  
TTHFMDEADLLGDRIAIMAKGELQCCGSSLFLKQKYGAGYHMTLVKEPHCNPEDISQLV  
HHHVPNATLESSAGAELSFILPRESTHRFEGLFAKLEKKQKELGASFGASITTMEEVFLR  
VGKLVDSMDIQAIQLPALQYQHERRASDWAVDSNLCGAMDPSDGIGALIEEERTAVKL  
NTGLALHCQQFWAMFLKKAAYSWREWKMVAAQVLVPLTCVTLALLAINYSSELFDDPM  
LRLTLGEYGRTVVPFSVPGTSQLGQQLSEHLKDALQAEGQEPREVLGDLEEFIFRASV  
EGGGFNERCLVAASFRDVGERTVVNALFNNQAYHSPATALAVVDNLLFKLLCGPHASIV  
VSNFPQPRSALQAAKDQFNEGRKGF DIALNLLFAMAFLASTFSILAVSERAVQAKHVQF  
VSGVHVASFWSALLWDLISFLIPSLLLLVVFKAFDVRAFTRDGHMADTLLLLLLYGWAI  
PLMYLMNFFFLGAATAYTRLTIFNILSGIATFLMVTIMRIPAVKLEELSKTLDHVFLVLPNH  
CLGMAVSSFYENYETRRYCTSSSEVAAHYCKKYNIQYQENFYAWSAPGVGRFVASMAA

SGCAYLILLFIETNLLQRLRGILCALRRRRTLTELYTRMPVLPEDQDVADERTRILAPSP  
 DSSLHTPLIIKELSKVYEQRVPLLAVDRLSLAVQKGECFLLGFNGAGKTTTFKMLTGEE  
 SLTSGDAFVGGHRISSDVGKVRQRIGYCPQFDALLDHMTGREMLVMYARLRGIPERHI  
 GACVENTLRGLLLEPHANKLVRTYSGGNKRKLSTGIALIGEPAVIFLDEPSTGMDPVARR  
 LLWDTVARARES GKAIITSHSMEECEALCTRLAIMVQQQFKCLGSPQHLKSKFGSGYSL  
 RAKVQSEGQQEALEEFKAFVDLTFPGSVLEDEHQGMVHYHLPGRDLSWAKVFGILEKA  
 KEKYGVDDYSVSQISLEQVFLSFAHLQPPTAEEGR

SEQID No:187

MAQALPWLLLWMGAGVLP AHGTQH GIRLPLRSGLG GAPLGLRLPRETDEEPEEPGRR  
 GSFVEMVDNLRGKSGQGYVEMTVGSPQTLNILDVTGSSNFAVGAAPHPFLHRYQQ  
 RQLSSTYRDLRKG VYVPYTQGK WEGELGTDLV SIPHGPNVTVRANIAAITESDKFFINGS  
 NWEGLGLAYAEIARPD DSLEPFFDSL VKQTHVPNLFSLQLCGAGFPLNQSEVLASVGG  
 SMIIGGIDHSLYTGSLWYTPIRREWYYEVIIVRVEINGQDLKMDCKEYNYDKSIVDSGTTN  
 LRLPKKVFEAAVKSIAASSTEKFPDGFWLGEQLVCWQAGTTPWNIFPVISLYLMGEVT  
 NQSFRTILPQQYL RPVEDVATSQDDCYKFAISQSSTGTVMGAVIMEGFYVVFDRARKRI  
 GFAVSACHVHDEFRTAAVEGPFVTLDMEDCGYNIPQTDESTLMTIAYVMAAICALFMLP  
 LCLMVCQWRCLRCLRQQHDDFADDISLLK

SEQID No:188

MSEADGLRQRRPLRPQVVTDDDGQAPEAKDGSSFSGRVFRVTFMLAVSLTVPLLGA  
 MMLLESPIDPQPLSFKEPPLLLGVLHPNTKLRQAERLFENQLVGPESIAHIGDVMFTGTA  
 DGRVVKLENGEIETIARFGSGPCKTRDDEPVCGRPLGIRAGPNGTLFVADAYKGLFEVN  
 PWKREVKLLLSSETPIEGKNMSFVNDLTVTQDGRKIYFTDSSSKWQRRDYLLLVMEGT  
 DDGRLLEYDTVTREVKVLLDQLRFPNGVQLSPAEDFVLVAETTMARIRRVYVSGLMKG  
 GADLFVENMPGFPDNIRPSSSGGYWVGMSTIRPNPGFSMLDFLSERPWIKRMIFKLFS  
 QETVMKFVPRYSLVLELSDSGAFRRSLHDPDGLVATYISEVHEHDGHLYLGSFRSPFLC  
 RLSLQAV

SEQID No:189

MLKVTVPSCSASSCSSVTASAAPGTASLVPDYWIDGSNRDALSDFFEVESELGRGATSI  
 VYRCKQKGTQKPYALKVLKKTVDKKIVRTEIGVLLRLSHPNIIKLKEIFETPTEISLVLELVT  
 GGELFDRIVEKGYYSERDAADAVKQILEAVAYLHENGIVHRDLKPENLLYATPAPDAPLK  
 IADFGLSKIVEHQVLMKTVCGTPGYCAPEILRG CAYGPEVDMWSVGIITYILLCGFEPFY

DERGDQFMFRILNCEYYFISPPWWDEVSLNAKDLVRKLIVLDPKKRLTTFQALQHPWVT  
 GKAANFVHMDTAQKKLQEFNARRKLKAAVKAVVASSRLGSASSSHGSIQESHKASRDP  
 SPIQDGNEDMKAIPERGEKIQGDGAQAQAVKGAQAELMKVQALEKVKGADINAEAPKMMV  
 PKAVEDGIKVADLELEEGLAEEKLKTVEEAAAPREGQGSSAVGFVPPQQDVILPEY

SEQID No:190

MSSSEEVSWISWFCGLRGNEFFCEVDEDYIQDKFNLTGLNEQVPHYRQALDMILDLEP  
 DEELEDNPNQSDLIEQAAEMLYGLIHARYILTNRGIAQMLEKYQQGDFGYCPRVYCENQ  
 PMLPIGLSDIPGEAMVKLYCPKCMDVYTPKSSRHHHTDGAYFGTGFPHMLFMVHPEYR  
 PKRPAHQFVPRLYGFKIHPMAYQLQLQAASNFKSPVKTIR

SEQID No:191

MWQLWASLCCLLVLANARSRPSFHPVSEDELVNYVNKRNTTWQAGHNFYNVDMSYLKR  
 LCGTFLGGPKPPQRMFTEDLKLPAFSDAREQWPQCPTIKEIRDQGSCGSCWAFGAV  
 EAISDRICHTNAHVSVEVSAEDLLTCCGSMCGDGCNGGYPAEAWNFWTRKGLVSGGL  
 YESHVGCRPYISIPPCEHHVNGSRPPCTGEGDTPKCSKICEPGYSPTYKQDKHYGYNSY  
 SVSNSEKDIMAIEYKNGPVEGAFSVYSDFLLYKSGVYQHVTGEMMGHHAIRILGWGVE  
 NGTPYWLANSWNTDWGDNGFFKILRGQDHCGIESEVVAGIPRTDQYWEKI

SEQID No:192

MMRQAPTARKTTTTRRPKPTRPASTGVAGASSSLGPSGSASAGELSSSEPSTPAQTPLA  
 APIIPTPVLTSFGAVPPLSPSPSKEEEGLRAQVRDLEEKLETLRKRAEDKAKLKELEKHKI  
 QLEQVQEWKSKMQEQQADLQRRLEKEARKEAKEALEAKERYMEEMADTADAIEMATLD  
 KEMAEERAESLQQEVEALKERVDELTTDLEILKAEIEEKGS DGAASSYQLKQLEEQNAR  
 LKDALVRMRDLSSEKQEHVKLQKLMEKKNQELEVVRQQRERLQEELSQAESTIDELK  
 EQVDAALGAEEMVEMLTDRNLNLEEKVRELRETVGDLEAMNEMNDELQENARETELEL  
 REQLDMAGARVREAQKRVEAAQETVADYQQTIKKYRQLTAHLQDVNRELTNQQEASV  
 ERQQQPPPETFDKIKFAETKAHAKAIEMELRQMEVAQANRHMSLLTAFMPDSFLRPG  
 GDHDCVLVLLMPRLICKAELIRKQAQEKFELSENCSERPGLRGAAGEQLSFAAGLVYS  
 LSLQATLHRYEHALSQCSVDVYKKVGS LYPMSAHERSLDFLIELLHKDQLDET VNV  
 PLTKAIKYYQHLYSIHLAEQPEDCTMQLADHIKFTQSALDCMSVEVGRLRAFLQGGQEA  
 TDIALLLRDLETSCSDIRQFCKKIRRRMPGTDAPGIPAALAFGPQVSDTLDCRKHLTWV  
 VAVLQEVAAAAAQLIAPLAENEGLLVAALEELAFKASEQIYGTPSSSPYECLRQSCNILIS  
 TMNKLATAMQEGEYDAERPPSKPPPVELRAAALRAEITDAEGLGLKLEDRETVIKELKK

SLKIKGEELSEANVRLSILLEKKLDSAAKDADERIEKVQTRLEETQALLRKKEKEFEETMD  
 ALQADIDQLEAEKAELKQRLNSQSKRTIEGLRGPPPSGIATLVSGIAGEEQQRGAIPGQA  
 PGSVPGPGLVKDSPLLLQQISAMRLHISQLQHENSILKGAQMKASLASLPPLHVAKLSHE  
 GPGSELPAGALYRKTSQLETLNQLSTHTHVVDITRTSPAAKSPSAQLMEQVAQLKSLS  
 DTVEKLDKDEVKQTVSQRPGATVPTDFATFPSSAFLRAKEEQQDDTVYMGKVTFSCAA  
 GFGQRHRLVLTQEQLHQLHSRLIS

## SEQID No:193

MGKGGNQGEAAEREVSVPFTSWEEIQKHNLRTDRWLVIDRKVYNITKWSIQHPGGQ  
 RVIGHYAGEDATDAFRAHPDLEFVGKFLKPLLIGELAPEEPSQDHGKNSKITEDFRALR  
 KTAEDMNLFKTNHVFFLLLLAHIIALESIAWFTVFYFGNGWIPTLITAFVLATSQAQAGWL  
 QHDYGHLSVYRKPKWNHLVHKFVIGHLKGASANWWNHRHFQHHAKPNIFHKDPDVNM  
 LHVFLGEWQPIEYGKKKLKYLPHNHQHEHYFFLIGPPLLIPMYFQYQIIMTMIVHKNWVDL  
 AWAVSYYIRFFITYIPFYGILGALLFLNFIRFLESHWFVWVTQMNHIVMEIDQEAYRDWFS  
 SQLTATCNVEQSFFNDWFSGHLNFQIEHHLFPTMPRHNLHAKIAPLVKSLCAKHGIEYQE  
 KPLLRAALLDIIRSLKKSGKLWLDAYLHK

## SEQID No:194

MASLDRVKVLVLGDSGVGKSSLVHLLCQNQVLGNPSWTVGCSVDVRVHDYKEGTREE  
 KTCYIELWDVGGSVGSASSVKSTRAVFYNSVNGIIFVHDLTNKKSSQNLRRWSLEALNR  
 DLVPTGVLVTNGDYDQEQFADNQIPLLIGTKLDQIHETKRHEVLTFTAFLAEDFNPEEIN  
 LDCTNPRYLAAGSSNAVKLSRFFDKVIEKRYFLREGNQIPGFPDRKRFGAGTLKSLHYD

## SEQID No:195

MNNHVSSKPSTMKLKHTINPILLYFIHFLISLYTILTYIPFYFFSESREQSNRIKAKPVNSK  
 PDSAYRSVNSLDGLASVLYPGCDTLDKVFTYAKNKFKNKRLLGTREVLNEEDEVPNG  
 KIFKKVILGQYNWLSYEDVFVRAFNFGNGLQMLGQKPKTNIAIFCETRAEWMIAAQACF  
 MYNFQLVTLYATLGGAIVHALNETEVTNIITSKELLQTKLKDIVSLVPRLRHIITVDGKPPT  
WSDFPKGIIVHTMAAVEALGAKASMENQPHSKPLPSDIAVIMYTSGSTGLPKGVMISHS  
 NIIAGITGMAERIPELGEEDVYIGYLPLAHVLELSAELVCLSHGCRIGYSSPQTLADQSSKI  
 KKGSKGDTSMKPTLMAAVPEIMDRIYKNVMNKVSEMSSFQRNLFILAYNYKMEQISKG  
 RNTPLCDSFVFRKVRSLGGINIRLLCGGAPLSATTQRFMNICCCPVGQGYGLTESAG  
 AGTISEVWDYNTGRVGAPLVCCEIKLKNWEEGGYFNTEKPHPRGEILIGGQSVTMGY  
 KNEAKTKADFSEDENGQRWLCTGDIGEFEPDGCLKIIDRKDLVKLQAGEYVSLGKVEA



ALKNLPLVDNICAYANSYHSYVIGFVVPNQKELTELARKKGLKGTWEELCNSCEMENEV  
LKVLSEAAISASLEKFEIPVKIRLSPEPWTPETGLVTDFAFKLRKELKTHYQADIERMYGR  
K

SEQID No:196

MKLKLNVLTIILLPVHLLITIYSALIFIPWYFLTNAKKKNAMAKRIKAKPTSDKPGSPYRSVT  
HFDSLAVIDIPGADTLDKLFDAVSKFGKKDSLGTREILSEENEMQPNGKVFKKLILGNY  
KWMNYLEVNRNRRVNNFGSGLTALGLKPKNTIAIFCETRAEWMIAAQTCFKYNFPLVTLYA  
TLGKEAVVHGLNESEASYLITSVELLESKLKTALLDISCVKHIIYVDNKAINKAEYPEGFEIH  
SMQSVEELGSPENLGIPPSRPTPSDMAIVMYTSGSTGRPKGVMHHSNLIAGMTGQ  
CERIPGLGPKDTYIGYLPLAHVLELTAEISCFTYGCRIGYSSPLTSLDQSSKIKKGSKGDC  
TVLKPTLMAAVPEIMDRIYKNVMSKVQEMNYIQKTLFKIGYDYKLEQIKKGYDAPLCNLLL  
FKKVKALLGGNVRMMLSGGAPLSPQTHRFMNVCFCCPIGQGYGLTESCGAGTVTEVT  
DYTTGRVGAPLICCEIKLKDWEQGGYTINDKPNPRGEIVIGGQNISMGYFKNEEKTAEDY  
SVDENGQRWFCTGDIGEFHPDGCLQIIDRKDLVKLQAGEYVSLGKVEAALKNCPLIDNI  
CAFAKSDQSYVISFVVPNQKRLTLLAQQKGVGTWVDICNNPAMEAEILKEIREAANAM  
KLERFEIPIKVRLSPEPWTPETGLVTDFAFKLRKELRNHYLKDIERMYGGK

SEQID No:197

MRRLTRRLVLPVFGVLWITVLLFFWVTKRKLEVPTGPEVQTPKPSDADWDDLWDQFDE  
RRYLNAKKWRVGDDPYKLYAFNQRESERISSNRAIPDTRHLSVLNRTPTHLIREIILVDDF  
SNPDDDCKQLIKLPKVKCLRNNERQGLVRSRIRGADIAQGTTLTFLDSHCEVNRDWLQP  
LLHRVKEDYTRVVCPVIDIINLDTFTYIESASELRGGFDWSLHFQWEQLSPEQKARRLDP  
TEPIRTPIIAGGLFVIDKAWFDYLGKYDMDMDIWGGGENFEISFRVWMCAGGSLEIVPCSRV  
GHVFRKKHPYVFPDGNANTYIKNTKRTAEVWMDEYKRYYYAARPFALERPFGNVESRL  
DLRKNLRCQSFKWYLENIYPELSIPKESSIQKGNIRQRQKCLESQANGTTGSSGQRPAG  
GTSEIWVQKPRVRNRRHAAPQGFDPGAKPSQHWRRPEHPAAE

SEQID No:198

MFFSMGFIVAVKGKIASPLEAPVFAAPHSTFFDGIACVVAGLPSMVSARNENAQVPLIGR  
LLRAVQPVLVSRVDPDSRKNTINEIIRTTSGGEWPQILVFPEGTCTNRSLITFKPGAFI  
PGVPVQPVLLRYPNKLDTVTWTWQGYTFIQLCMLTFCQLFTKVEVEFMPVQVPNDEEK  
NDPVLFAKVRNLMAEALGIPVTDHTYEDCRLMISAGQLTLPMEAGLVEFTKISRKLKLD  
WDGVRKHLDEYASIASSSKGGRIIEEFAKYLKLPVSDVLRQLFALFDRNHDGSIDFREY

VIGLAVLCNPSNTEEEIQVAFKLFVDVDEDDGYITEEEFSTILQASLGVPDLVDVSGLFKEIAQG  
 DSISYEEFKSFALKHPEYAKIFTTYLDLQTCHEVFSLPKEVQTTTPSTASNKVSPEKHEEST  
 SDKKDD

SEQID No:199

MRPRRPHQIADLFRPKDQIAYSDTSPFLILSEASLADLNSRLEKKVKATNFRPNIVISGCD  
 VYAEDSWDELLIGDVELKRVMACSRCILTTVDPDTGVMSRKEPLETLKSYRQCPSERK  
 LYGKSPLFGQYFVLENPGTIKVGDPVYLLGQ

SEQID No:200

MSSFGYRTLTVALTFLICCPGSDEKVFEVHVRPKKLAVEPKGSLEVNCSTTCNQPEVGG  
 LETSLNKILLDEQAQWKHYLVSNISHDTVLQCHFTCSGKQESMNSNVSVYQPPRQVILT  
 LQPTLVAVGKSFTIECRVPTVEPLDSLTLFLFRGNETLHYETFGKAAPAPQEATATFNST  
 ADREDGHRNFSCLAVLDLMSRGGNIFHKHSAPKMLEIYEPVSDSQMVIIVTVVSVLLSLF  
 VTSVLLCFIFGQHRLRQQRMGTYGVRAAWRRLPQAFRP

SEQID No:201

MDTEGFGELLQQAELAAETEGISELPHVERNLEIQQAGERLRSRTLTRTSQETADV  
 ASVLLGSRGLDISHISQRLESLSAATTFEPLPVKDTDIQGFLKNEKDNALLSAIEESRKR  
 TFGMAEEYHRESMLVEWEQVKQRILHTLLASGEDALDFTQESEPSYISDVGPGRSSL  
 DNIEMAYARQIYIYNEKIVNGHLQPNLVDLCASVAELDDKSISDMWTMVKQMTDVLLTPA  
 TDALKNRSSVEVRMEFVRQALAYLEQSYKNYTLVTVFGNLHQAQLGGVPGTYQLVRSF  
 LNIKLPAPLPGLQDGEVEGHPVWALIYYCMRCGDLLAASQVNVRAQHQLGEFKTWFE  
 YMNSKDRRLSPATENKLRLHYRRALRNNTDPYKRAVYCIIGRCDVTDNQSEVADKTED  
 YLWLKLNQVCFDDDGTSPPQDRLTLSQFQKQLLEDYGESHTVNQQPFLYFQVFLTA  
 QFEAAVAFLFRMERLRCHAVHVALVLFELKLLLKSSGQSAQLLSHEPGDPPCLRRNLNFV  
 RLLMLYTRKFESTDPREALQYFYFLRDEKDSQGENMFLRCVSELVIESREFDMILGKLE  
 NDGSRKPGVIDKFTSDTKPIINKVASVAENKGLFEEAAKLYDLAKNADKVLELMNKLLSP  
 VVPQISAPQSNKERLKNMALSIAERYRAQGISANKFVDSTFYLLDLITFFDEYHSGHIDR  
 AFDIERLKLVLNQUESVEERVAAFRNFSDEIRHNLSEVLLATMNILFTQFKRLKGTSPSS  
 SSRPQRVIEDRDSQLRSQARTLITFAGMIPYRTSGDTNARLVQMEVLMN

SEQID No:202

MLLVLECVLFSSVAQGYFRMDSSATQFHIETHENTSGLWSIWYRNHFDRSVVLNDVFLSK

ETKHMLKILNFTGPLFLPPGCWNIFSLKLAVKDIAINLFTNVFLTNNIGAIFAIPLOIYSAPTK  
 EGSLGFEVIAHCGMHYFMGKSKAGNPWNWNGSLSLDQSTWNVDSELANKLYERWKKY  
 KNGDVCKRNVLGTTTFAHLKKSKESESFVFFLPRLIAEPGLMLNFSATALRSRMIKYFVV  
 QNPSSWPVSLQLLPLSLYPKPEALVHLLHRWFGTDMQMINFTTGEFQLTEACPYLGTH  
 SEESRFGILHLHLQPLEMKRVGVVFTPADYGKVTSLILIRNNLTVIDMIGVEGFGARELLK  
 VGGRLPGAGGSLRFKVPESTLMDCRRQLKDSKQILSITKNFKVENIGPLPITVSSLKINGY  
 NCQGYGFEVLDCHQFSLDPNTSRDISIVFTPDTSSWVIRDLSLVTAADLEFRFTLNVTL  
 PHLLPLCADVVPGPSWEESFWRLTVFFVSLSLLGVLIAFQQAQYILMEFMKTRQRQN  
 ASSSSQQNNGPMDVISPHSYKSNCKNFLDTYGPSDKGRGKNCLPVNTPQSRIQNAAK  
 RSPATYGHSHQKKHKCSVYYSKHKTSTAAASSTSTTTEEKQTSPLGSSSLPAAKEDICTDA  
 MRENWISLRYASGINVNLQKNLTLPKNLLNKEENTLKNTIVFSNPSSECSMKKEGIQTCMF  
 PKETDIKTSENTAEFKERELCPLKTSKKLPENHLPRNSPQYHQPDLPESRKNNNGNNQQ  
 VPVKNEVDHCENLKKVDTKPSSEKKIHKTSREDMFSEKQDIPFVEQEDPYRKKKLQEK  
 EGNLQNLNWSKSRTCRKNKRGVAPVSRPPEQSDLKLVCSDFERSELSSDINVRSWCI  
 QESTREVCKADAEIASSLPAAQREAEGYYQKPEKKCVDFKFCSDSSSDCGSSSGSVRAS  
 RGSWGSWSSTSSSDGDKKPMVDAQHFLPAGDSVSQNDPSEAPISLNLSHNICNPMT  
 VNSLPQYAEPSCPSLPAGPTGVEEDKGLYSPGDLWPTPPVCVTSSLNCTLENGVPCVI  
 QESAPVHNSFIDWSATCEGQFSSAYCPLLENDYNAFPEENMNYANGFPCPADVQTDFI  
 DHNSQSTWNTPPNMPAAWGHASFISSPPYLTSTRSLSPMSGFLGSIWAPQSDVYENC  
 CPINPTTEHSTHMENQAVVCKEYYPGFNPFRAVMNLDIWTTTANRNANFPLSRDSSYC  
 GNV

SEQID No:203

ASGEWRVSGGRPAGAGRPEEALAAGSDPRGAAARLACSAPTPGGGTMPFDFFRRFDIY  
 RKVPKDLTQPTYTGAIISICCLFILFLFLSELTFITTEVVNELYVDDPDKDSGGKIDVSL  
 NISLPNLHCELVGLDIQDEMGRHEVGHIDNSMKIPLNNGAGCRFEGQFSINKVPGNFHV  
 STHSATAQPQNPDMTHTVHKLSFGDTLQVQNIHGAFNALGGADRLTSNPLASHDYILKIV  
 PTVYEDKSGKQRYSYQYTVANKEYVAYSHTGRIIPAIWFRYDLSPITVKYTERRQPLYRF  
 ITTICAIIGGTFTVAGILDSCIFTASEAWKKIQLGKMH

SEQID No:204

NSKKMQSWYSMLSPTYKQRNEDFRKLFSKLPEAERLIVDYSCALQREILLQGRLYLSEN  
 WICFYSNIFRWETTISIQLKEVTCLKKEKTAKLIPNAIQICTESEKHFFTSFGARDRCFLIF  
 RLWQNALLEKTLSPRELWHLVHQCYGSELGLTSEDEDYVSPLQLNGLGTPKEVGDVIA

LSDITSSGAADRSQEPPSPVGSRRGHVTPNLSRASSDADHGAEEDKEEQVDSQPDASS  
 SQTVTPVAEPPSTEPTQPDGPTTLGPLDLLPSEELLTDTSNSSSSTGEEADLAALLPDL  
 GRLLINSVFHVGAERLQQMLFSDSPFLQGFLQQCKFTDVTLSPWSGDSKCHQRRVLT  
 TIPISNPLGPKSASVVETQTLFRRGPQAGGCVVDSEVLTQGIPYQDYFYTAHRYCILGLA  
 RNKARLRVSSEIRYRKQPWSLVKSLIEKNSWSGIEDYFHHLERELAKAEKLSLEEGGKD  
 ARGLLSGLRRRRKRPLSWRAHGDGPQHPDPDPCARAGIHTSGSLSSRFSEPSVDQGP  
 AGIPSALVLISIVSLIILIALNVLLFYRLWSLERTAHTFESWHSALAKGKFPQTATEWAEIL  
 ALQKQFHSVEVHKWRQILRASVELLDKMFSLKHLHQGITVSDPPFDTPQPRPDDSF

SEQID No:205

MLGLLVALLALGLAVFALLDVWYLVRLPCAVLRARLLQPRVRDLLAEQRFPGRVLP  
 DLLLHMNNARYLREADFARVAHLTRCGVLGALRELRAHTVLAASCARHRRSLRLLPEF  
 VRTRLLGWDDRAFYLEARFVSLRDGFVCALLRFRQHLLGTSPERVVQHLCCRRVEPPE  
 LPADLQHWISYNEASSQLLRMESGLSDVTKDQ

SEQID No:206

MTLARFVLALMLGALPEVVGFDSVLNDSLHSHRHSPAGPHYPPYLLPTQQRPPPTTRP  
 PPPLPRFPRPPRALPAQRPHALQAGHTPRPHPWGPCPAGEPWVSVTDFGAPCLRWAE  
 VPPFLERSPPASWAQLRGQRHNFCSRSPDGAGRPWCFYGDARGKVDWGYCDCRHGS  
 VRLRGKNEFEGTVEVYASGVWGTVCSSHWDDSDASVICHQLQLGGKGIKQTPFSG  
 LGLIPIYWSNVRCRGDEENILLCEKDIWQGGVCPQKMAAAVTCSFSHGPTFPRIIRLAGGS  
 SVHEGRVELYHAGQWGTVCDDQWDDADADEVICRQLGLSGIAKAWHQAYFGEGSGPV  
 MLDEVRCCTGNELSIEQCPKSSWGEHNCGHKEDAGVSCTPLTDGVIRLAGGKGSHEGR  
 LEVYYRGQWGTVCDDGWTELNTYVVCRLGLGFKYKQASANHFEESTGPIWLDDVSCS  
 GKETRFLQCSRRQWGRHDCSHREDVSIACYPGGEGHRLSLGFPVRLMDGENKKEGR  
 VEVFINGQWGTICDDGWTDKDAAVICRQLGYKGPARARTMAYFGEGKGPIHVDNVKCT  
 GNERSLADCIKQDIGRHNCRHSEDAGVICDYFGKKASGNSNKESSLSSVCGLRLLHRRQ  
 KRIIGGKNSLRGGWPWQVSLRLKSSHGDGRLLCGATLLSSCWVLTAAHCFKRYGNSTR  
 SYAVRVGDYHTLVPEEFEEEEIGVQQIVIHREYRPDRSDYDIALVRLQGPEEQCARFSSH  
 VLPACLPLWRERPQKTASNCYITGWGDTGRAYSRTLQQAAPLLPKRFCEERYKGRFT  
 GRMLCAGNLHEHKRVDSCQGDSGGPLMCERPGEWVVGVTWGYGCGVKDSPGV  
 YTKVSAFVPWIKSVTKL

SEQID No:207

MEDGGLTAFEEDQRCLSQSLPLPVSAEGPAAQTAEPSRSFSSAHRHLSRRNGLSRLC  
 QSRTALSEDRWSSYCLSSLAQNICTSKLHCPAAPEHTDPSEPRGSVSCCSLLRGLSS  
 GWSSPLLPAVPCNPKNKAIFTVDAKTTEILVANDKACGLLGYSSQDLIGQKLTQFFLRSDS  
 DVVEALSEEHMEADGHAADVFGTVVDIISRSGEKIPVSVWMKRMQRERRLCCVVVLEP  
 VERVSTWVAFQSDGTVTSCDSLFAHLHGYVSGEDVAGQHITDLIPSVQLPPSGQHIPKN  
 LKIQRSVGRARDGTTFPLSLKLKSQPSSEEATTGEAAPVSGYRASVWVFCTISGLITLLP  
 DGTIHGINHSFALTTFGYGKTELLGKNITFLIPGFYSYMDLAYNSSLQLPDLASCLDVGNE  
 SGCGERTLDPWQGQDPAEGGQDPRINVVLGGHVPRDEIRKLMEQDIFTGTQTELI  
 AGGQLLSCLSPQPAPGVDNVPEGSLPVHGEQALPKDQQTALGREEPVAIESPGQDLL  
 GESRSEPVDVKPFASCEDSEAPVPAEDGGSDAGMCGLCQKAQLERMGVSGPSGSDL  
 WAGAAVAKPQAKGQLAGGSLLMHCPCYGSEWGLWWRSDQLAPSPSGMAGLSFGTP  
 TLDEPWLGVENDREELQTCLIKEQLSQLSLAGALDVPHAELVPTCEQAVTAPVSSCDLG  
 GRDLCGGCTGSSSACYALATDLPGGLEAVEAQEVDVNSFSWNLKELFFSDQTDQTSS  
 NCSCATSELRETPSSLAVGSDPDVGSLSQEQGSCVLDDRELLLLTGTCVDLGQGRRFRE  
 SCVGHDPTPELEVCLVSSEHYAASDRESPGHVPSTLDAGPEDTCPSAEEPRLNVQVTS  
 TPVIVMRGAAGLQREIQEGAYSGSCHHRDGLRLSIQFEVRRVELQGPTPLFCCWLVD  
 LLHSQRDSAARTRLFLASLPGSTHSTAELTGPSLVEVLRARPWFEEPPKAVELEGLAA  
 CEGEYSQKYSTMSPLGSGAFGFVWTAVDKEKNKEVVVKFIKKEKVLEDCWIEDPKLGK  
 VTLEIAILSRVEHANIIVLDIFENQGFFQLVMEKHGSGLDLFAFIDRHPRLDEPLASYIFR  
 QLVSAVGYLRKDIHRDIKDENVIAEDFTIKLIDFGSAAYLERGKLFYTFCGTIEYCAPEV  
 LMGNPYRGPELEMWSLGVTLTYLVFEENPFCELEETVEAAIHPPYLVSKEMLSLVSGLL  
 QPVPERRTTLEKLVTDPWVTQPVNLADYTWEVCRVKNKPESGVLSAASLEMGNRSL  
 DVAQAQELCGGPVPGAPNGQGCLHPGDPRLTS

SEQID No:208

MEPGTGGSRKRLGPRAGFRFWPPFFPRRSQAGSSKFPTPLGPENSGNPTLLSSAQPE  
 TRVSYWTKLLSQLLAPLPGLLQKVLWSQLFGGMFPTRWLDFAGVYSALRALKGREKP  
 APTAQKSLSSLQLDSSDPSVTSPLDWLEEGIHWQYSPPDLKLELKAKGSALDPAAQAF  
 LLEQQLWGVELLPSLQSRLYSNRELGSSPSGPLNIQRIDDFSVMVSYLLNPSYLDLCPRL  
 EVSYQNSDGNSEVVGFQTLTPESSCLREDHCHPQPLSAELIPASWQGCPLSTEGLPEI  
 HHLRMKRLEFLQQASKGQDLPTPDQDNGYHSLEEEHSLLRMDPKHCRDNPTQFVPAA  
 GDIPGNTQESTEEKIELLTTEVPLALEEESPSSEGCPSSSEIPMEKEPGEGRISVVDYSYLE  
 GDLPIARPACSNKLIDYILGGASSDLETSSDPEGEDWDEEAEDDGFSDSSSLSDSDLE

QDPEGLHLWNSFCSDPYNPQNFTATIQTAAARIVPEEPSDSEKDLGKSDLENSSSQSG  
SLPETPEHSSGEEDDWESSADEAESLKLWNSFCNSDDPYNPLNFKAPFQTSGENEKG  
CRDSKTPSESIVAISECHTLLSCKVQLLGSQESECPDSVQRDVLSGGRHTHVKRKKVTF  
LEEVTEYYISGDEDRKGPWEEFARDGCRFQKRIQETEDAIGYCLTFEHRERMFNRLQG  
TCFKGLNVLKQC

SEQID No:209

MNLERSVNEEKLNLCKRYLGGFAFLPFLWLVNIFWFFREAFPLVPAYTEQSQIKGYVWR  
SAVGFLFWVIVLTSWITIFIYRPRWGALGDYLSFTIPLGTP

SEQID No:210

MTELPAPLSYFQNAQMSEDNHLNNTNDNRERQEHNDRRSLGHPEPLSNGRPQGNSR  
QVVEQDEEEDDEELTKYGAKHVIMLFVPVTLCMVVVVATIKSVSFYTRKDGQLIYTPFTE  
DTETVGQRALHSILNAAIMISVIVVMTILLVVLYKYRCYKVIHAWLISSLLLLFFFSFIYLGE  
VFKTYNVAVDYITVALLIWNLGVVGMISIHWKGPLRLQQAYLIMISALMALVFIKYLPEWT  
AWLILAVISVYDLVAVLCPKGPLRMLVETAQERNETLFPALIYSSTMVWLVNMAEGDPEA  
QRRVSKNSKYNAESTERESQDTVAENDDGGFSEWEAQRDShLGPHERSTPESRAAV  
QELSSSILAGEDPEERGVLGLGDFIFYSVLVGKASATASGDWNTTIACFVAILIGLCLTL  
LLLAIFKKALPALPISITFGLVFYFATDYLVQPFMDQLAFHQFYI

SEQID No:211

MAAETLLSSLLGLLLLGLLLPASLTGGVGSLNLEELSEMRYGIEILPLPVMGGQSQSSDV  
VIVSSKYKQRYECRLPAGAIHFQREREEETPAYQGPGIPELLSPMRDAPCLLTKDWWT  
YFCYGRHIQQYHMEDSEIKGEVLYLGYQSAFDWDDetakASKQHRLKRYHSQTYG  
NGSKCDLNGRPREAEVRFLCDEGAGISGDYIDRVDEPLSCSYVLTIRTPRLCPHPLLRP  
PPSAAPQAILCHPSLQPEEY MAYVQRQADSKQYGDKIIIEELQDLGPQVWSETKSGVAP  
QKMAGASPTKDDSKDSDFWKMLNEPEDQAPGGEEVPAEEQDPSPEAADSASGAPND  
FQNNVQVKVIRSPADLIRFIEELKGGTKKGKPNIGQE QPVDDAAEVPQREPEKERGDPE  
RQREMEEEEEDEDEDEDEDERQLLGEFEKELEGILLPSDRDRLRSEVKAGMERELN  
IIQETEKELDPDGLKKESERDRAMLALTSTLNKLIKRLKQSPVDDAAEVPQREPEKERGDPE  
PPSPQPTTEEDPEHRVRVRVTKLRLGGPNQDLTVLEMKRENPLKQIEGLVKELLEREG  
LTAAGKIEIKIVRPWAEGTEEGARWLTD DTRNLKEIFFNILVPGAEAAQKERQQRQKELE  
SNYRRVWGSPGGEGTGDLDEFDF

## SEQID No:212

MAVVPLLLLGGGLWSAVGASSLGVVTCGSVVKLLNTRHNVRLHSHDVRYGSGSGQQSV  
TGVTSVDDSNSYWRIRGKSATVCERGTPIKCGQPIRLTHVNTGRNLHSHHFTSPLSGN  
QEVSAFGEEGEGDYLDWTVLCNGPYWVRDGEVRFKHSSTEVLVSVTGEQYGRPISG  
QKEVHGMAQPSQNNYWKAMEGIFMKPSELLKAEAHHAEL

## SEQID No:213

MEASGKLICRQRQVLFSFLLLGLSLAGAAEPRSYSVVEETEGSSFVTNLAKDLGLEQRE  
FSRRGVRVVSRRGNKLHLQLNQETADLLLNEKLDREDLCGHTEPCVLRQVLLESPPFEFF  
QAEQVIDINDHSPVFLDKQMLVKVSESSPPGTAFPLKNAEDLDIGQNNIENYIISPNSYF  
RVLTRKRSRDKRYPPELVLDNALDREEEAELRLTLTALDGGSPPRSGTAQVYIEVVDVND  
NAPEFQQPFYRVQISEDSPISFLVVKVSATDVDVTGVNGEISYSLFQASDEISKTFKVDFLT  
GEIRLKKQLDFEFQSYEVNIEARDAGGFSGKCTVLIQVIDVNDHAPEVTMSAFTSPIPE  
NAPETVVALFSVSDLDSENGKISCSIQEDLPFLKSSVGNFYTLTETPLDRESRAEYN  
VTITVTDLGTPLTTHLNMTVLVSDVNDNAPAFQTSTYTLFVRENNSPALHIGSVSATDR  
DSGTNAQVTYSLLPPQDPHLPLASLVSTNDNGHLFALRSLDYELQAFEFVRVGASDRG  
SPALSSEALVRVLVDANDNSPFVLYPLQNGSAPCTELVPRAAEPGYLVTKVVAVDGDS  
GQNAWLSYQLLKATEPGLFGVWAHNGEVRTARLLSERDAAKQRLVVLVKDNGEPPCS  
ATATLHLLLVDGFSQPYLPLPEAAPAQGQADSLTVYLVVALASVSSLFLFSVLLFVAVLLC  
RRSRAASVGRCSVPEGPFGHLVDVRGTGSLSQNYQYEVCLAGGSGTNEFQFLKPVL  
PNIQGHSGPEMEQNSNFRNGFGFSLQLK

## SEQID No:214

MASRGVVGIFFLSAVPLVCLELRRGIPDIGIKDFLLCGRILLLLALLTLISVTTSWLNSFKS  
PQVYLKEEEEKNEKRQKLVRKKQQEAQGEKASRYIENVLKPHQEMKLRKLEERFYQMT  
GEAWKLSSGHKLGGDEGTSQTSFETSNREAAKSQNLKPLTEFPSPAQPTCKEIPDL  
PEEPSQTAEVVTVALRCPSGNVLRRRFLKSYSSQVLFDWMTRIGYHISLYSLSTSFP  
RPLAVEGGQSLEDIGITVDTVLILEEKEQTN

## SEQID No:215

MAAAEEEDGGPEGPNRERGGAGATFECNICLETAREAVSVCGHLYCWPCLHQWLET  
RPERQECPVCKAGISREKVVPLYGRGSQKPQDPRLKTPPRPQGQRPAPESRGGFQPF  
GDTGGFHFSFGVGAFPGFFFTTVFNAHEPFRRGTGVDLGQGHPASSWQDSLFLFLAIF  
FFFWLLSI

SEQID No:216

MKFLLDILLLLPLLIVCSLESFVKLFIPKRRKSVTGEIVLITGAGHGIGRLTAYEFAKLKSKL  
VLWDINKHGLEETAACKCKGLGAKVHTFVVDCSNREDIYSSAKKVKAIEIGDVSILVNNAGV  
VYTSDLFATQDPQIEKTFEVNVLAHFWTTKAFLPAMTKNNHGHIVTVASAAGHVSVPFLL  
AYCSSKFAAVGFHKTLTDELAALQITGVKTTCLCPNFVNTGFIKNPSTSLGPTLEPEEVV  
NRLMHGILTEQKMIFIPSSIAFLTTLERILPERFLAVLKRKISVKFDAVIGYKMKQAQ

SEQID No:217

MWSAGRGGAAWPVLLGLLLALLVPGGGAAKTGAELVTCGSVLKLLNTHHRVRLHSHDI  
KYGSGSGQQSVTGVEASDDANSYWRIRGGSEGGCPCGSPVRCGQAVRLTHVLTGKN  
LHTHHFPSPLSNNQEVSFAFGEDGEGDDLDLWTVRCSGQHWEREAAVRLQHVGTSVFL  
SVTGEQYGSPIRGQHEVHGMP SANTHNTWKAMEGIFIKPSVEPSAGHDEL

SEQID No:218

GRWASGEMAPSGSLAVPLAVLVLLLWGAPWTHGRRSNVRVITDENWRELLEGDWMIE  
FYAPWCPACQNLQPEWESFAEWGEDLEVNIKVDVTEQPGLSGRFIITALPTIYHCKDG  
EFRRYQGPRTKKDFINFISDKEWKSI EPVSSWFGPGSVLMSSMSALFQLSMWIRTCHN  
YFIEDLGLPVWGSYTVFALATLFSGLLLGLCMIFVADCLCPSKRRRPQYPYPYPSKKLLSE  
SAQPLKKVEEEQEAEDEEDVSEEEEAESKEGTNKDFPQNAIRQRS LGPSLATDKS

SEQID No:219

HPAGLAAAAAGTPRLPSKRRIPVSQPGMADPHQLFDDTSSAQSRGYGAQRAPGGLSY  
PAASPTPHA AFLADPVSNMAMAYGSSLAAQGKELVDKNIDRFIPITKLKYYFAVD TMYV  
GRKLGLLFFPYLHQDWEVQYQQDTPVAPRFDVNAPDLYIPAMAFITYVLVAGLALGTQD  
RFSPDLLGLQASSALAWLTLEVLAILLSLYLVTVNTDLTTIDLVAFLGYKYVGMIGGVLMG  
LLFGKIGYYLVLGWCCVAIFVFMIRTLRLKILADAAAEGVPVRGARNQLRMYLTMAVAAA  
QPMLMYWLTFHLVR

SEQID No:220

MAATALLEAGLARVLFYPTLLYTLFRGKVPGRAHRDWYHRIDPTVLLGALPLRSLTRQLV  
QDENVRGVITMNEEYETRFLCNSSQEWKRLGVEQLRLSTVDMTG IPTLDNLQKGVQFA  
LKYQSLGQC VYVHCKAGRSRSATMVAAYLIQVHKWSPEEAVRAIAKIRSYIHIRPGQLDV  
LKEFHKQITARATKDGT FVISKT



SEQID No:221

MNTVLSRANSLFAFSLSVMAALTFGCFITTAFAKDRSVPVRLHVSRIMLKNVEDFTGPRER  
 SDLGFITSDITADLENIFDWNVKQLFLYLSEAESTKNNALNQVVLWDKIVLRGDNPKLLK  
 DMKTKYFFFDDGNGLKGNRNVTLTWSNVVPNAGILPLVTGSGHVSVPFPDYEITKSY

SEQID No:222

MALRGFCSADGSDPLWDWNVTWNTSNPDFTKCFQNTVLVWVPCFYLWACFPFYFLYL  
 SRHDRGYIQMTPLNKTKTALGFLLWIVCWADLFYSFWERSRGIFLAPVFLVSPTLLGITT  
 LLATFLIQLERRKGVQSSGIMLTFWLVALVCALAILRSKIMTALKEDAQVDLFRDITFYVYF  
 SLLLIQLVLSCFSDRSPLFSETIHDPNPCPESSASFLSRITFWWITGLIVRGYRQPLEGSD  
 LWSLNKEDTSEQVVPVLVKNWKKECAKTRKQPVKVYSSKDPAQPKESSKVDANEEV  
 EALIVKSPQKEWNPSLFKVLYKTFGPYFLMSFFFKAIHDLMMFSGPQILKLLIKFVNDTKA  
 PDWQGYFYTVLLFVTACLQTLVLHQYFHICFVSGMRIKTAVIGAVYRKALVITNSARKSS  
 TVGEIVNLMSVDAQRFMDLATYINMIWSAPLQVILALYLLWNLGPSVLAGVAVMVLMVP  
 VNAVMAKTKTYQVAHMKSKDNRIKLMNEILNGIKVLKLYAWELAFKDKVLAIRQEELKV  
 LKKSAYLSAVGTFTWVCTPFLVALCTFAVYVTIDENNILDAQTAFVSLALFNILRFPLNILP  
 MVISSIVQASVSLKRLRIFLSHEELEPDSIERRPVKDGGGTNSITVRNATFTWARSDPPTL  
 NGITFSIPEGALVAVVGQVGCCKSSLLSALLAEMDKVEGHVAIKGVNLSSGGQKQRVSLA  
 RAVYSNADIYLFDDPLSAVDAHVGKHIFENVIGPKGMLKNKTRILVTHSMSYLPQVDVIIV  
 MSGGKISEMGSYQELLARDGAFAEFLRTYASTEQQEQAEEENGVTGVSGPGKEAKQME  
 NGMLVTD SAGKQLQRQLSSSSSYSGDISRHHNSTAELQKAEAKKEETWKLMEADKAQ  
 TGQVKLSVYWDYMKAI GLFISFLSIFLMCNHVSALASNYWLSLWTD DPVNGTQEHTK  
 VRLSVYGALGISQGI AVFGYSMAVSIGGILASRCLHVDLLHSILRSPMSFFERTPSGNLVN  
 RFSKELDTVD SMIP EVIKMF MGSLFNVIGACIVILLATPIAAIIIPPLGLIYFFVQRFYVASSR  
 QLKRLSVSRSPVYSHFNETLLGVSVIRAFEEQERFIHQSDLKVDENQKAYYPSIVANR  
 WLAVRLECVGNCIVLFAALFAVISRHSL SAGLVGLSVSYSLQVTTYLNWLVRMSSEMET  
 NIVAVERLKEYSETEKEAPWQIQETAPPSSWPQVGRVEFRNYCLRYREDLDFVLRHINV  
 TINGGEKVGIVGRTGAGKSSLTLGLFRINESAEGEIIIDGINIAKIGLHDLRFKITIIPQDPVLF  
 SGSLRMNLDPFSQYSDEEVWTSLELAHLKDFVSALPDKLDHECAEGGENLSVGQRQLV  
 CLARALLRKT KILVLDEATAAVDLETDDLIQSTIRTQFEDCTVLTIAHRLNTIMDYTRVIVLD  
 KGEIQEYGAPSDLLQQRGLFY SMAKDAGLV

SEQID No:223

MARGKAKEEGSWKKFIWNSEKKEFLGRTGGSWFKILLFYVIFYGCLAGIFIGTIQVMLLTI  
SEFKPTYQDRVAPPGLTQIPQIQKTEISFRPNDPKSYEAYVLNIVRFLEKYKDSAQRDDM  
IFEDCGDVPSEPKERGDFNHERGERKVCRFKLEWLGNCSSLNDETYGYKEGKPCIIKL  
NRVLGFKPKPPKNESLETYPVMKYNNPNVLPVQCTGKRDEDDKDKVGNVEYFGLGNSPG  
FPLQYYPPYYGKLLQPKYLQPLLAVQFTNLTMDTEIRIECKAYGENIGYSEKDRFQGRFDV  
KIEVKS

SEQID No:224

MKVARFQKIPNGENETMIPVLTSKKASELPVSEVASILQADLQNLNKCEVSHRRAFHG  
WNKFDISEDEPLWKKYISQFKNPLIMLLLASAVISVLMHQFDDAVSITVAILIVTVAFVQE  
YRSEKSLEELSKLVPPECHCVREGKLEHTLARDLVPGDTVCLSVGDRVPADLRLFEAVD  
LSIDESSLTGETTPCSKVTAQPAATNGDLASRSNIAFMGTLVRCGKAKGVVIGTGENS  
EFGEVFKMMQAEAEAPKTPLQKSMDLLGKQLSFYSFGIIGIIMLVGWLLGKDILEMFTISVS  
LAVAAIPEGLPIVTVTLALGVMRMVKKRAIVKKLPIVETLGCCNVICSDKTGTLTKNEMT  
VTHIFTS DGLHAEVTGVGYNQFGEVIVDGDVVHGFYNPAVSRIVEAGCVCNDAVIRNNT  
LMGKPTEGALIALAMKMGLDGLQQDYIRKAEYPFSSEQKWMMAVKCVHRTQQDRPEICF  
MKGAYEQVIKYCTTYQSKGQTLTLTQQQRDVYQQEKARMGSAGLRVLALASGPPELGQ  
LTFLGLVGII DPPRTGVKEAVTTLIASGVSIKMITGDSQETAVAIASRLGLYSKTSQSVSGE  
EIDAMDVQQLSQIVPKVAVFYRASPRHKMKIISLQKNGSVVAMTGDGVNDAVALKAAD  
IGVAMGQTGTDVCKEADMILVDDDFQTIMSAIEEGKGIYNNIKNFVRFQLSTSI AALTIS  
LATLMNFPNPLNAMQILWINIIMDGPPAQLSGVEPVDKDVIRKPPRNWKDSILTKNLILKIL  
VSSIIIVCGTLFVFWREL RDNVITPRDTTMTFTCFVFFDMFNALSSRSQTKSVFEIGLCSN  
RMFCYAVLGSIMGQLLVIYFPPLQKVFQTESLSILDLLFLLGLTSSVCIVAEIHKVERSRE  
KIQKHVSSTSSSFLEV

SEQID No:225

MAKNRRDRNSWGGFSEKTYEWSSEEEEPVKKAGPVQVLIVKDDHSFELDETALNRILL  
SEAVRDKEVVAVSVAGAFRKGKSFLMDFMLRYMYNQESVDWVG DYNEPLTGFSWRG  
GSERETTGIQIWSEIFLINKPDGKKVAVLLMDTQGT FDSQSTLRDSATVFALSTMISSIQV  
YNLSQNVQEDDLQHLQLFTEYGR LAMEETFLKPFQSLIFLVRDWSFPYEF SYGADGGA  
KFLEKRLKVSGNQHEELQNVRKHIHSCFTNISCFLLPHPG LKVATNP NFDGKLKEIDDEFI  
KNLKILIPWLLSPESLDIKEINGNKITCRGLVEYFKAYIKIYQGEELPHPKSMLQATAEANN  
LAAVATAKDTYNKKMEEICGGDKPFLAPNDLQTKHLQLKEESVKLFRGVKKMGGEFFS

RRYLQQLESEIDELYIQYIKHNDSKNIFHAARTPATLFVVIFITYVIAGVTGFIGLDIIASLCN  
MIMGLTLITLCTWAYIRYSGEYRELGAVIDQVAAALWDQGSTNEALYKLYSAAATHRHLY  
HQAFTPKESESTEQSEKKKM

SEQID No:226

MGCCSSASSAAQSSKREWKPLEDRSCTDIPWLLLILFCIGMGFIGFSIATGAAARLVS  
GYDSYGNICGQKNTKLEAIPNSGMDHTQRKYVFFLDPCNLDLINRKIKSVALCVAACPR  
QELKTLSDVQKFAEINGSALCSYNLKPSEYTTSPKSSVLC PKLPVPASAPIFFHRCAPV  
NISCYAKFAEALITFVSDNSVLHRLISGVMTSKEIILGLCLLSVL SMILMVIIIRYISRVLVWIL  
TILVILGSLGGTGVLWWLYAKQRRSPKETVTPEQLQIAEDNLRALLIY AISATVFTVILFLIM  
LVMRKRVALTIALFHVAGKVFIHLPLL VFQPFWTF FALVLFWVYWIMTLLFLGTTGSPVQ  
NEQGFVEFKISGPLQYMWVYHVGLIWSEFILACQMQMTVAGAVVTYYFTRDKRNLPFT  
PILASVNRILIRYHLGTVAKGSFIITLVKIPRMILMYIHSQKKGKENACARCVLKSCICCLWC  
LEKCLNYLNQNAYTATAINSTNFCTSAKDAFVILVENALRVATINTVGDFMLFLGKVLIVC  
STGLAGIMLLNYQQDYTVWVPLIIVCLFAFLVAHCFLSIYEMVVDVLF LCF AIDTKYNDG  
SPGREFYMDKVLMEFVENS RKAMKEAGKGGVADSRELKPMLKKR

SEQID No:227

EKSGGPGTREEREREKREERQSAWGRKERGREGWVRRRERSAANPRRRRAWSPSQNS  
SPSRSRSQGGGCRDRQPCMMHLRLFCILLAAVSGAEGWGYG CDEELVGPLYARSLG  
ASSYYSLLTAPRFARLHGISGWSPRIGDPNPWLQIDLMKKHRIRAVATQGSFNSWDWV  
TRYMLLYGDRVDSWTPFYQRGHNSTFFGNVNESAVVRHDLHFHFTARYIRIVPLAWNP  
RGKIGRLRLGLYGCPYKADILYFDGDDAISYRFPRGVSRSRLWDVFAFSFKTEEKDGLLLHA  
EGAQGDYVTLELEGAHLLLHMSLGSSPIQPRPGHTTVSAGGVLNDQHWYVRVDRFG  
RDVNFTLDGYVQRFILNGDFERLNLDT E MFIGGLVGAARKNLAYRHNFRGCIENVIFNRV  
NIADLAVRRHSRITFEGKVAFRCLDPVPHPI NFGGPHNFVQVPGFPRRGRLAVSFRFRT  
WDLTGLLLFSRLGDGLGHVELT LSEGQVNVSIAQSGRKKLQFAAGYRLNDGFWHEVNF  
VAQENHAVISIDDVEGAEVRVSYPLLIRTGTSYFFGGCPKPASRWDCHSNQTA FHGCM  
ELLKVDGQLVNLT LVEGRRLGFYAEVLFDTCGITDR CSPNMCEHDGRCYQSWDDFICY  
CELTGYKGETCHTPLYKESCEAYRLSGKTSGNFTIDPDGSGPLKPFV VYCDIRENRAWT  
VVRHDLRWTTTRVTGSSMERPFLGAIQYWNASWEEVSALANASQHCEQWIEFSCYNSR  
LLNTAGGY PYSFWIGRNEEQHFYWGGSQPGIQRACGLDRSCVDPALYCNC DADQPQ  
WRTDKGLLTFVDHLPVTQVVIGDTNRSTSEAQFFLRPLRCYGDRNSWNTISFHTGAALR  
FPPIRANHSLDVSFYFRTSAPSGVFLENMGGPYCQWRRPYVRVELNTSRDVVFAFDVG

NGDENLTVHSDDFEFNDDEWHLVRAEINVKQARLRVDHRPWVLRPMPPLQTYIWMEYD  
 QPLYVGS AELKRRPFV GCLRAMRLNGVTLNLEGRANASEGTSPNCTGHCAHPRLPCF  
 HGGRCVERYSYTCDCLTA FDGPYCNHDIGGFFEPGTWMRYNLQSALRSAAREFSH  
 MLSRPVPGYEPGYIPGYDTPGYVPGYHGPYRLPDYPRPGRPVPGYRGPVYNVTGEE  
 VSFSFSTSSAPAVLLYVSSFVRDYM AVLIKDDGTLQLRYQLGTSPYVYQLTTRPVTDGQ  
 PHSINITRVYRNLFIQVDYFPLTEQKFSL LVDSQLDSPKALYLGRVMETGVIDPEIQRYNT  
 PGFSGCLSGVRFNNAVPLKTHFRTPRPM TAEALAEALRVQGELSESNCGAMPRLVSEVP  
 PELDPWYLPPDFPYHDEGWVAILLGFLVAFLLLGLVGMLVLFYLQNHRYKGSYHTNEP  
 KAAHEYHPGSKPPLPTSGPAQVPTPTAAPNQAPASAPAPAPTAPAPGPRDQNL PQIL  
 EESRSE

SEQID No:228

MGNRGMEDLIPLVNRLQDAFSAIGQNADLDLPQIAVVGGQSAGKSSVLENFVGRDFLP  
 RSGSIVTRRPLVLQLVNATTEYAEFLHCKGKKFTDFEEVRLEIEAETDRVTGTNKGISPV  
 PINLRVYSPHVLNLTLDLPGMTKVPVGDQPPDIEFQIRDMLMQFVTKENCLILAVSPAN  
 SDLANS DALKVAKEVDPQGQRTIGVITKLDLMDEGTDARDVLENKLLPLRRGYIGVVNR  
 SQKDIDGKKDITAALAAERKFFLSHPSYRHLADRMGTPYLQKVLNQQLTNHIRD TLPGLR  
 NKLQSQLLSIEKEVEEYKNFRPDDPARKTKALLQM VQQFAVD FEKRIEGSGDQIDTYEL  
 SGGARINRIFHERFPFELVKMEFDEKELRREISYAIKNIHGIRTGLFTPDMAFETIVKKQVK  
 KIREPCLKCVD M VISELISTVRQCTKKLQQYPR LREEMERIVTTHIREREGRTKEQVM LLI  
 DIELAYMNTNHEDFIGFANAQQRSNQMNKKKTSGNQDEILVIRKGWLTINNIGIMKGGSK  
 EYWFVLTAENLSWYKDDEEKEKKYMLSVDNLKLRDVEKGMSSKHIFALFNTEQRNVY  
 KDYRQLELACETQEEVDSWKASFLRAGVYPERVGDKEKASETEENGSDSFMHSM DPQ  
 LERQVETIRNLVDSYMAIVNKTVRDLMPKTIMHLMINNTKEFIFSELLANLYSCGDQNTLM  
 EESAEQAQRRDEMLRMYHALKEALSII GNINTTTVSTPMPPPVD DSWLQVQSV PAGRR  
 SPTSSPTPQRRAPAVPPARPGSRGPAPGPP PAGSALGGAPPVPSRPGASPD PFGPPP  
 QVPSRPNRAPPGVPSRSGQASPSRPESPRPPFDL

SEQID No:229

MAARRQGPARSANPRPQFPGVCGREHAATLRAPGRGGGASPAQIGTRGRGGHNFAP  
 NLTARSAVTSGLGPPAAVMVGS LNCIVAVSQNMGIGKNGDLPWPPLRNEFRYFQRM  
 TTTSSVEGKQNLVIMGKKTWFSIPEKNRPLKGRINLVLSRELKEPPQGAHFLSRSLDDAL  
 KLTEQPELANKVDMVWIVGGSSVYKEAMNHPGHLKLFVTRIMQDFESDTFFPEIDLEKY  
 KLLPEYPGVLSDVQEEKGIKYKFEVYEKND

SEQID No:230

MDRGTLPLAVALLLASCSLSPTSLSAETVHCDLQPVGPERGEVITYTTTSQVSKGCVAQAP  
 NAILEVHVLFLFPTGPSQLELTLQASKQNGTWPREVLLVLSVNSSVFLHLQALGIPLHL  
 AYNSSLVTFQEPPGVNTTELPSFPKTQILEWAAERGPITSAAELNDPQSILLRLGQAQGS  
 LSFCMLEASQDMGRTLLEWRPRTPALVRGCHLEGVAGHKEAHILRVLPGHSAGPRTVTV  
 KVELSCAPGDLDVILQGGPPYVSWLIDANHNMQIWTTGEYSFKIFPEKNIRGFKLPDTP  
 QGILLGEARMLNASIVASFVELPLASIVSLHASSCGGRLQTSPAPIQTTPPKDTCSPELLM  
 SLIQTCKADDAMTLVLKKELVAHLKCTITGLTFWDPSCEAEDRGDKFVLRSAVSSCGMQ  
 VSASMISNEAVVNILSSSSPQRKKVHCLNMDLSLQGLYLSPHFLQASNTIEPGQQSF  
 VQVRVSPSVSEFLLQLDSCHLDLGPEGGTVELIQGRAAKGNCVSLSPSPEGDPFRFSFL  
 LHFYTVPIPKTGTLSCTVALRPKTGSQDQEVHRTVFMRLNIISPDLSGCTSKGLVLPVL  
 GITFGAFLIGALLTAALWYIYSHTRSPSKREPVVAVAAPASSESSSTNHSIGSTQSTPCST  
 SSMA

SEQID No:231

MCASVKYNIRGPALIPRMKTKHRIYYITLFSIVLLGLIATGMFQFWPHSIESSNDWNVEKR  
 SIRDVPVVRLPADSPIPERGDLSCRMHTCFDVYRCGFNPKNKIKVYIYALKKYVDDFGVS  
 VSNTISREYNELMAISDSYYTDDINRACLFVPSIDVLNQNTLRIKETAAQAMAQLSRWD  
 RGTNHLLFNMLPGGPPDYNTALDVPRDRALLAGGGFSTWYRQGYDVSIPVYSPLSAE  
 VDLPEKGPGRQYFLLSSQVGLHPEYREDLEALQVKHGESVLVLDKCTNLSEGVLSVR  
 KRCHKHQVFDYPQVLQEATFCVVLRGARLGQAVLSDVLQAGCVPVVIADSYILPFSEVL  
 DWKRASVVPEEKMSDVYSILQSIPQRQIEEMQRQARWFWEAYFQSIKAIATLQIIND  
 RIYPYAAISYEEWNDPPAVKWGSVSNPLFLPLIPPQSQGFTAIVLTDRVESLFRVITEVS  
 KVPSLSKLLVWNNQNKNPPEDSLWPKIRVPLKVVRTAENKLSNRFFPYDEIETEAVLAI  
 DDDIIMLTSDLEQFGYEVWREFPDRLVGYPGRLHLWDHEMNKWKYESEWTNEVSMVL  
 TGAAFYHKEYFNLYTYKMPGDIKNWVDAHMCNCDIAMNFLVANVTGKAVIKVTPRKFKF  
 CPECTAIDGLSLDQTHMVERSEKINKFASVFGTMPLKVVEHRADPVLYKDDFPEKLSF  
 PNIGSL

SEQID No:232

MTGYTMLRNGGAGNGGQTCMLRWSNRIRLTWLSFTLFVILVFFPLIAHYLTTLDEADE  
 AGKRIFGPRVGNELCEVKHVLDCRIRESVSEELLQLEAKRQELNSEIAKLNKIEACKKS  
 IENAKQDLLQLKNVISQTEHSYKELMAQNQPKLSLPIRLLPEKDDAGLPPPKATRGCRHLH

NCFDYSRCPLTSGFPVYVYDSQFVFGSYLDPLVKQAFQATARANVYVTENADIACLYV  
 ILVGEMQEPVVLRPAAELEKQLYSLPHWRTDGHNHVIINLSRKSDTQNLLYNVSTGRAMV  
 AQSTFYTVQYRPGFDLVVSPLVHAMSEPNFMEIPPQVPVKRKYLFTFQGEKIESLRSSL  
 QEARSFEEEMEGDPPADYDDRIIATLKAVQDSKLDQVLVEFTCKNQPKPSLPTIEWALC  
 GEREDRLELLKLSTFALIITPGDPRLVISSGCATRLFEALEVGAVPVVLGEQVQLPYQDM  
 LQWNEAALVVPKPRVTEVHFLLRSLSDSLLAMRRQGRFLWETYFSTADSIFNTVLAMI  
 RTRIQUIPAAPIREEAAAEIPHRSGKAAGTDPNMADNGDLDLGPVETEPYASPRYLNRFT  
 LTVTDFYRSWNCAPGPFHLFPHTPFDPVLPSEAKFLGSGTGFRPIGGGAGGSGKEFQA  
 ALGGNVPREQFTVVMLTYEREEVLMNSLERLNLPLYLNKVVVWVNSPKLPSEDLLWPD  
 IGVPIMVVRTEKNSLNNRFLPWNEIETAILSIDDDAHLRHDEIMFGFRVWREARDRIVGF  
 PGRYHAWDIPHQSWLYNSNYSCELSMVLTGAFFHKYAYLYSYVMPQAIRDMVDEYI  
 NCEDIAMNFLVSHITRKPIKVTSRWTFRCPGCPQALSHDDSHFHERHKCINFFVKVYG  
 YMPLLYTQFRVDSVLFKTRLPHDKTKCKFI

SEQID No:233

MGPGRPAPAPWPRHLLRCVLLLGCLHLGRPGAPGDAALPEPNVFLIFSHGLQGCGLEAQ  
 GGQVRVTPACNTSLPAQRWKWVSRNRLFNLTGMQCLGTGWPGTNTTASLGMYECDR  
 EALNLRWHCRTLGDQLSLLLGARTSNISKPGTLERGDQTRSGQWRIYGSEEDLCALPY  
 HEVYTIQGNSHGKPCITPFKYDNQWFHGGCTSTGREDGHLWCATTQDYGKDERWGF  
 PIKSNDCETFWDKDQLTDSCYQFNQSTLSWREAWASCEQQGADLLSITEIHEQTYING  
 LLTGYSSTLWIGLNDLDTSGGWQWSDNSPLKYLNWESDQPDNPSEENCGVIRTESSG  
 GWQNRDCSIALPYVCKKKPNATAEPTPPDRWANVKVECEPSWQPFQGHYCYRLQAEK  
 RSWQESKKACLRGGGDLVSIHSMAELEFITKQIKQEVEELWIGLNDLKLQMNFEWSDG  
 SLVSFTHWHHPFEPNNFRDSLEDCVTIWGPEGRWNDSPCNQSLPSICKKAGQLSQGAA  
 EEDHGCRKGWTWHSPSCYWLGEDQVTYSEARRLCTDHGSQVLVTITNRFEQAFVSSLI  
 YNWEGEYFWTALQDLNSTGSFFWLSGDEVMYTHWNRDQPGYSRGGCVALATGSAM  
 GLWEVKNCTSFARYICRQSLGTPVTPPELPGPDPTPSLTGSCPQGWASDTKLRYCYKV  
 FSSERLQDKKSWVQAQAGACQELGAQLLSLASYEEHFVANMLNKIFGESEPEIHEQHW  
 FWIGLNRRDPRGGQSWRWSDGVGFSYHNFDNRHDDDDIRGCAVLDLASLQWVAMQ  
 CDTQLDWICKIPRGTDVREPDDSPQGRREWLRFEAEYKFFEHHSTWAQAQRICWTF  
 QAELTSVHSQAELDFLSHNLQKFSRAQEQHWWIGLHTSESDGRFRWTDGSIINFISWA  
 PGKPRPVGKDKKCVYMTASREDWGDQRCLTALPYICKRSNVTKETQPPDLPTTALGG  
 CPSDWIQFLNKCFQVQGQEPQSRVKWSEAQFSCEQQAQLVTITNPLEQAFITASLPN  
 VTFDLWIGLHASQRDFQWVEQEPLMYANWAPGEPSPGSPAPSGNKPTSCAVVLHSPS

AHFTGRWDDRSCTEETHGFICQKGTDPSSLSPSPAALPPAPGTELSYLNGTFRLLQKPLR  
 WHDALLLCESHNASLAYVPDPYTQAFLTQAARGLRTPLWIGLAGEEGSRRYSWVSEEP  
 LNYVGWQDGEPPQQPGGCTYVDVDGAWRTTSCDTKLQGA VCGVSSGPPPPRRISYHG  
 SCPQGLADSAWIPFREHCYSFHMELLGHKEARQRCQRAGGAVLSILDEMENVFVWE  
 HLQSYEGQSRGAWLGMNFPKGGTLVWQDNTAVNYSNWGPPGLGPSMLSHNSCYW  
 IQSNSGLWRPGACTNITMGVCKLPRAEQSSFSPSALPENPAALVVVLMVLLLLALLTA  
 ALILYRRRQSIERGAFEGARYSRSSSSPTTEATEKNILVSDMEMNEQQE

SEQID No:234

MEDHQHVPIDIQTSKLLDWLVDRRHCSLKWQSLVLTIREKINAAIQDMPESSEEIAQLLSG  
 SYIHYPFHCLRILDLLKGTEASTKNIFGRYSSQRMKDWQEIIALYEKDNITYLVELSSLLVRN  
 VNYEIPSLKKQIAKCQQLQQEYSRKEEEECQAGAAEMREQFYHSCCKQYGITGENVRGEL  
 LALVKDLPSQLAEIGAAAQQSLGEAIDVYQASVGVFCESPTQVLPMLRFVQKRGNSTV  
 YEWRTGTEPSVVERPHLEELPEQVAEDAIDWGDGVEAVSEGTDSGISAEAAAGIDWGI  
 FPESDSKDPGGDGIDWGDDAVALQITVLEAGTQAPGVARGPDALTLLEYTETRQFL  
 DELMELEIFLAQRAVELSEEADVLSVSQFQLAPAILQGQTKMKMTMVSVLEDLIGKLTS  
 LQLQHLMILASPRYVDRVTEFLQQKLKQSLLALKKELMVQKQQEAL EEQAALPKLD  
 LLEKTKELQKLIADISKRYSGRPVNLMGTSL

SEQID No:235

MDTSRLGVLLSLPVLLQLATGGSSPRSGVLLRGCPHCHCEPDGRMLLRVDCSDLGLS  
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 MLQNNQLRHVPTEALQNLRLSLRLDANHISYVPPSCFSGLSRLHLWLDNALTEIP  
 VQAFRSLSALQAMTLALNKIHHIPDYAFGNLSSLVVLHLHNNRIHSLGKKCFDGLHSLET  
 LDLNYYNNLDEFPTAIRTLNLKELGFHSNNIRSIPEKAFVGNPSLITIFHYDNPIQFVGRSA  
 FQHLPELRTLTLNGASQITEFPDLTG TANLES LT LTGAQISSLPQTVCNQLPNLQVLDLSY  
 NLLEDLPFSVCQKLQKIDLRHNEIYEIKVDTFQQLSLRSLNLAWN KIIHPNAFSTLPS  
 LIKDLSSNLLSSFPITGLHGLTHLKL TGNHALQSLISSENFPELKVIEMPYAYQCCAFGV  
 CENAYKISNQWNKGDNSSMDDLHKKDAGMFQAQDERDLEDFLD FEEDLKALHSVQC  
 SPSPGPFKPCHELLDGWLIRIGVWTIAVLALTCNALVTSTVFRSPLYISPIKLLIGVIAAVN  
 MLTGVS SA VLAGVDAFTFGSFARHGAWWENG VGVCHVIGFLSIFASESSVFLTLAALER  
 GFSVKYSAKFETKAPFSSLKVIILLCALLALTMAAVPLLGGSKYGASPLCLPLPFGEPTM  
 GYMVALILLNSLCFLMMTIAYTKLYCNLDKGDLENIWDCSMVKHIALLLFTNCILNCPVAF

LSFSSLINLTFISPEVIKIFILLVVVPLPACLNPLLYILFNPHFKEDLVSLRKQTYVWTRSKHP  
SLMSINSDDVEKQSCDSTQALVTFTSSSITYDLPPSSVPSPAYPVTESCHLSSVAFVPCL

SEQID No:236

MIASHLLAYFFTELNHDQVQKVDQYLYHMRLSDETLLEISKRFRKEMEKGLGATTHPTA  
AVKMLPTFVRSTPDGTEHGEFLALDLGGTNFRVLWVKVTDNGLQKVEMENQIYAIPEDI  
MRGSGTQLFDHIAECLANFMDKLQIKDKKLPLGFTFSFPCHQTKLDESFLVSWTKGFKS  
SGVEGRDVVALIRKAIQRRGDFDIDIVAVVNDTVGTMMTCGYDDHNCEIGLIVGTGSNA  
CYMEEMRHIDMVEGDEGRMCINMEWGAFGDDGSLNDRTEFDQEIDMGSLNPGKQLF  
EKMISGMYMGELVRLILVKMAKEELLFGGKLSPELLNTGRFETKDISDIEGEKDGIRKAR  
EVLMLRLGLDPTQEDCVATHRICQIVSTRSASLCAATLAAVLQRIKENKGEERLRSTIGVD  
GSVYKKHPHFAKRLHKTVRRLVPGCDVRFLRSEDGSGKGAAMVTAVAYRLADQHRAR  
QKTLEHLQLSHDQLLEVKRRMKVEMERGLSKETHASAPVKMLPTYVCATPDGTEKGDF  
LALDLGGTNFRVLLVRVRNGKWGGVEMHNKIYAIPQEVMMHGTGDELFDHIVQCIADFLE  
YMGMKGVSLPLGFTFSFPCQQNSLDESILLKWTGKFKASGCEGEDVVTLLKEAIHRREE  
FDLDVVAVVNDTVGTMMTCGFEDPHCEVGLIVGTGSNACYMEEMRNVELVEGEEGRM  
CVNMEWGAFGDNGCLDDFRTEFDVAVDELSLNPBKQRFKEMISGMYLGEIVRNILIDFT  
KRGLLFRGRISERLKTRGIFETKFLSQIESDCLALLQVRATLQHLGLESTCDDSIIVKEVCT  
VVARRAAQLCGAGMAAVVDRIENRGLDALKVTVGVDGTLYKLHPHFAKVMHETVKDL  
APKCDVSFLQSEDGSGKGAALITAVACRIREAGQR

SEQID No:237

CDGQPDCADGSDEWDCSYVLPRKVITA AVIGSLVCGLLLVIALGCTCKLYAIRTQEYSIF  
APLSRMEAEIVQQQAPPSYGQLIAQGAIPPVEDFPTENPNDNSVLGNLRSLLQILRQDM  
TPGGGPGARRRQRGRMLMRRLVHRLRRWGLLPRTNTPARASEARSQVTPSAAPLEALD  
GGTGPAREGGAVGGQDGEQAPPLPIKAPLPSASTSPAPTTVPEAPGPLPSLPLEPSLLS  
GVVQALRGRLLPSLGPPTSPGPHTAVLALEDEDDVLLVPLAEPGVWVAEAEDEP  
LLT

SEQID No:238

VTIAFLRLITTLVKGQLGSTQSQGLVPCVMFVLKEMLP SYHKWRYNSHGVREQIGCLILE  
LIHAILNLCHETDLHSSHTPSLQFLCICSLAYTEAGQTVINIMGIGVDITIDMVMAAQPRSD  
GAEGQQGQGQLLIKTVKLAFSVTNNVIRLKPPSNVVSPLEQALSQHGAGNNLIAVLAKYI  
YHKHDPALPRLAIQLLKRLATVAPMSVYACLGNDAAAIRDAFLTRLQSKIEDMRIKVMILE



FLTVAVETQPGLIELFLNLEVKDGS DGSKEFSLGMWSCLHAVLELIDSQQQDRYWCPPL  
 LHRAAIAFLHALWQDRRDSAMLVLRTPKPKFWENLTSPLFGTLPSPSETSEPSILETCALI  
 MKIICLEIYYVVKGS LDQSLKDTLKKFSIEKR FAYWSGYVKS LAVHVAETEGSSCTSLEY  
 QMLVSAWRMLLIATTHADIMHLTDSVVRRLFLDVLDTGKALLVPASVNCLRLGSMKC  
 TLLILLRQWKRELGSVDEILGPLTEILEGVLQADQQLMEKTKAKVFSAFITVLQMKEMKV  
 SDIPQYSQVLVNV CETLQEEVIALFDQTRHSLALGSATEDKDSMETDDCSRSRHRDQR  
 DGVCVLGLHLAKELCEVDEDGDSWLQVTRRLPILPTLLTTLEVSLRMKQNLHFTEATLHL  
 LLTLARTQQGATAVAGAGITQSICLPLLSVYQLSTNGTAQTPSASRKS LDAPSWPGVYR  
 LSMSLMEQLLKT LRYNFLPEALDFVGVHQERTLQCLNAVRTVQSLACLEEADHTVGFIL  
 QLSNFMKEWHFHL PQLMRDIQVGAQDGVLESGVMLGDREAVRSHWGTPSELQDVPE  
 RGLFPWGAQGLLSCAYSG

SEQID No:239

MWERLNCAAEDFYSRLLQKFNEEKKGIRKDPFLYEADVQVQLISKGQPNPLKNILNENDI  
 VFIVEKVPLEKEETSHIEELQSEETAISDFSTGENVGPLALPVGKARQLIGLYTMAHNPN  
 MTHLKINLPVTALPPLWVRCDSSDPEGTCWLGAELITTNNSITGIVLYVVSCKADKNYSV  
 NLENLKNLHKKRHHLSTVTSKGFAQYELFKSSALDDTITASQTAIALDISWSPVDEILQIP  
 PLSSTATLNIKVESGEPRGPLNHLYRELKFLVLADGLRTGVTEWLEPLEAKSAVELVQE  
 FLNDLNKLDGFGDSTKKDTEVETLKHDTAAVDRSVKRLFKVRSDLDFAEQLWCKMSSS  
 VISYQDLVKCFTLIIQSLQRGDIQPWLHSGSNSLLSKLIHQSYHGTMDTVSLSGTIPVQML  
 LEIGLDKLLKDYISFFIGQELASLNHLEYFIAPSVDIQEQVYRVQKLHHILEILVSCMPFIKS  
 QHELLFSLTQICIKYYKQNPLDEQHIFQLPVRPTAVKNLYQSEKPQKWRVEIYRGQKKIK  
 TVWQLSDSSPIDHLNFHKPDFSELTLNGSLEERIFFTNMVTCSQVHFK

SEQID No:240

MPGMVLFGRRWAIASDDLVPFGFFELVVRVLWWIGILTLYLMHRGKLD CAGGALLSSYL  
 IVLMILLAVVICTVS AIMCVSMRG TICNPGPRKSM SKLLYIRLALFFPEMVWASLGAAWVA  
 DGVQCDRTVVNGIATVVVSWIIIAATVVSIIIVFDPLGGKMAPYSSAGPSHLD SHDSSQLL  
 NGLKTAATSVWETRIKLLCCCIGKDDHTRVAFSSTAELFSTYFSDTDLVPSDIAAGLALLH  
 QQQDNIRNNQEP AQVVCHAPGSSQEADLDAELENCHHYMQFAAAAYGWPLYIYRNPL  
 TGLCRIGGDCCRSRTTDYDLVGGDQLNCHFGSILHTTGLQYRDFIHVSFHDKVYELPFL  
 VALDHRKESVVVAVRGTM SLQDVLTDLSAESEVLDVECEVQDRLAHKGISQAARYVYQ  
 RLINDGILSQA FSIAP EYRLVIVGHSLGGGAAALLATMLRAAYPQVRCYAFSPPRGLWSK  
 ALQEYSQS FIVSLVLGKDVIPRLSVTNLEDLKRRILRVVAHCNKPKYKILLHGLWYELFGG

NPNNLPTELDGGDQEVLTQPLLGEQSLLTRWSPAYSFSSDSPLDSSPKYPPLYPPGRII  
HLQEEGASGRFGCCSAAHYSAKWSHEAEFSKILIGPKMLTDHMPDILMRALDSVVSDR  
AACVSCPAQGVSSVDVA

SEQID No:241

MSSKEVKTALKSARDAIRNKEYKEALKHCKTVLKQEKNNNYNAWVFIGVAAAELEQPDQA  
QSAYKKAEELEPDQLLAWQGLANLYEKYNHINAKDDLPGVYQKLLDLYESVDKQKWCD  
VCKKLVDLYYQEKKHLEVARTWHKLIKTRREQGAENEELHQLWRKLTQFLAESTEDQN  
NETQQLLFTAFENALGLSDKIPSEDHQVLYRHFIIQSLSKFPHESARLKKACEGMINIYPTV  
QYPLEVLCLHLIESGNLTDEGQQYCCRLVEMDSKSGPGLIGLGIKALQDKKYEDAVRNL  
TEGLKESPVCTSGWYHLAEAQVKMHRPKEAVLSCSQALKIVDNLGASGNSLYQRNLCL  
HLKAEALIKLSDYDSSEEAIRTLQISDADNIPGLLVLKSLAYRNKGSFDEAAKIMEDLLSS  
YPDLAEVHALEALIHFTKKDYLAQAEKCFQRALEKDEVAEYHYQLGLTYWFMGEETRKD  
KTKALTHFLKAARLDTYMGKVFCYLGHYRVDVVGDKNRARGCYRKAFELDDTDAESGA  
AAVDLSVELEDMEMALAILTTVTQKASAGTAKWAWLRRGLYYLKAGQHSQAVADLQAA  
LRADPKDFNCWESLGEAYLSRGGYTTALKSFTKASELNPESIYSVFKVAAIQQILGKYKE  
AVAQYQMIKKKEDYVPALKGLGECHLMMAKAALVDYLDGKAVDYIEKALEYFTCALQH  
RADVSCWLKLAGDACTCLYAVAPSKVNVHVLGVLLGQKEGKQVLKKNELLHLGGRCY  
GRALKLMSTSNWCDLGINYYRQAQHLAETGSNMNDLKELLEKSLHCLKKAVRLDSNN  
HLYWNALGVVACYSIGIGNYALAQHCFIKSIQSEQINAVAWTNLGVLYLTNENIEQAHEAF  
KMAQSLDPSYLMCWIGQALIAEAVGSYDTMDLFRHTTELNMHTEGALGYAYWVCTTLQ  
DKSNRETELYQYNILQMNAIPAAQVILNKYVERIQNYAPAFTMLGYLNEHLQLKKEAANA  
YQRAILLQTAEDQDTYNVAIRNYGRLLCSTGEYDKAIQAFKSTPLEVLEDIIGFALALFM  
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QALCALGLAMQDATLSKAALNELLKHIKHKDSNYQRCLLTSIYALQGRSVAVQKQISKA  
VHSNPGDPALWSLLSRVVAQYAQRNAKGGVVAGNVAHILDSNHGKKALLYTAVNQLA  
MGSSSAEDEKNTALKTIQKAALLSPGDPAIWAGLMAACHADDKLALVNNTQPKRIDLYL  
ALLSAVSASIKDEKFFENYNQSLEKWSLSQAVTGLIDTGRISEAETLCTKNLKSNDPQPA  
VILLRQVQCKPLLESQKPLPDAVLEELQKTVMSNSTSVPAWQWLAHVYQSQGMMRA  
AEMCYRKSLQLASQRGSWSGKLSSLLRLALLALKVCMANISNDHWPSLVQEATTEALK  
LCFCPLAVLLQALLQFKRKMGAETRRLLERVVYQPGYPKSIASTARWYLLRHLYAKDD  
YELIDVLVNNNAKTHGDTRALELNQRLSSQ

SEQID No:242

MGAAAGRSPHLGPAPARRPQRSLLLLQLLLLVAAPGSTQAQAAPFPELCSYTWEAVDT  
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 DQQGTNHRVQSSIAFLCGKTLGTPEFVTATECVHYFEWRTTAACKKDIFKANKEVPCYV  
 FDEELRKHDLNPLIKLSGAYLVDDSDPDTSLFINVCRDIDTLRDPGSQLRACPPGTAACL  
 VRGHQAFDVGQPRDGLKLVRKDLVLSYVREEAGKLDFCDGHSPAVTITFVCPSERRE  
 GTIPKLTAKSNCRYEIEWITEYACHRDYLESKTCSLSGEQQDVSIDLTPLAQSGGSSYIS  
 DGKEYLFYLNVCGETEIQFCNKKQAAVCQVKKSDTSQVKAAGRYHNQTLRYSDGDLTLI  
 YFGGDECSSGFQRM SVINFE CNKTAGNDGKGTPVFTGEVDCTYFFTWDTEYACVKEK  
 EDLLCGATDGKKRYDLSALVRHAEPEQNWEAVDGSQTETEEKHFFINICHRVLQEGKA  
 RGCPEDAAVCAVDKNGSKNLGKFISSPMKEKGNIQLSYSDGDDCGHGKKIKTNITLVCK  
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 KNGAYKVETKKYDFYINVCGPVSVSPCQPD SGACQVAKSDEKTWNLGLSNAKLSYD  
 GMIQLNRYRGGTPYNNERHTPRATLITFLCDRDAGVGFPEYQEEDNSTYNFRWYTSYAC  
 PEEPLECVVTD PSTLEQYDLSSLAKSEGGLGGN WYAMDNSGEHVTWRKYI NVCRPL  
 NPVPGCNRYASACQMKYEKDQGSFTEVVSISNLGMAKTGPVVEDSGSLLLEYVNGSA  
 CTTSDGRQT TYTTRIHLVCSRGR LNSHPIFSLNWE CVVSFLWNTEAACPIQTTTDTDQA  
 CSIRDPN SGFVFNLNPLNSSQGYNVSGIGKIFMFNVCGTMPVCGTILGKPASGCEAETQ  
 TEELKNWKPARPVGIEKSLQLSTEGFITLTYKGPLSAKGTADAFIVRFVCNDDVYSGPLK  
 FLHQDIDSGQGIRNTYF EFETALACVPSPVDCQVTDLAGNEYDLTGLSTVRKPWTAVDT  
 SVDGRKRTFYLSVCNPLPYIPGCQGS AVGSCLVSEGN SWNLGVVQMSPQAAANGSLSI  
 MYVNGDKCGNQRFSTRITFECAQISGSPAFQLQDGCEYVFIWRTVEACP VVRVEGDNC  
 EVKDPRHGNLYDLKPLGLNDTIVSAGEYTY YFRVCGKLSSDVCPTSDKSKVVSSCQEK  
 REPQGFHKVAGLLTQKLTYENGLLKMNFTGGDTCHKVYQRSTAIFFYCDRGTQRPVFL  
 KETSDCSYLF EWRTQYACPPFDLTECSFKDGAGNSFDLSSLSRYSDNWEAITGTGDPE  
 HYLINVCKSLAPQAGTEPCPPEAAACLLGGSKPVNLGRVRDGPQWRDGIIVLKYVDGDL  
 CPDGIRKKSTTIRFTCS ESQVNSRPMFISAVEDCEYTFAWPTATACPMKSNEHDDCQVT  
 NPSTGHLFDLSSL SGRAGFTAAYSEKGLVYMSICGENENCPPGVGACFGQTRISVGKA  
 NKRLRYVDQVLQLVYKDGSPCPSKSGLSYKSVISFVCRPEAGPTNRPMLISLDKQTCTL  
 FFSWHTPLACEQATECSVRNGSSIVDLSPLIHRTGGYEAYDESEDDASDTNPDFYINIC  
 QPLNPMHAVPCPAGAAVCKVPIDGPPIDIGRVAGPPILNPIANEIYLN FESSTPCLADKHF  
 NYTSLIAFHCKRGVSMGTPKLLRTSECD FVFEWETPVVCPDEV RMDGCTLTDEQLLYS  
 FNLSSLSTSTFKVTRDSRTYSVGVCTFAVGPEQGGCKDGGVCLLSGTKGASFGRLQS  
 MKLDYRHQDEAVVLSYVNGDRCP PETDDGVPCVFPFIFNGKSYEECIIESRAKLWCSTT

ADYDRDHEWGF CRHSNSYRTSSII FKDEDEDIGRPQVFSEVRGCDVTFEWKTKV VCP  
 PKKLECKFVQKHKTYDLRLLSSLTGSWSLVHNGVSYIINLCQKIYKGPLGCSERASICR  
 RTTTGDVQVLGLVHTQKLGVIQDKVVVTYSGGYPCGGNKTASSVIELTCTKTVGRPAFK  
 RFDIDSCTYYFSWDSRAACAVKPQEVQMVNGTITNPINGKSFSLGDIYFKLFRASGDMR  
 TNGDNYLYEIQ LSSITSSRN PACSGANICQVKPNDQHFSRKVGTS DTKY YLQDGDLDV  
 VFASSSKCGKDKTKSVSSTIFFHCDPLVEDGIPEFSHETADCQYLFSWYTSAVCPLGVG  
 FDSENPGDDGQMHKGLSERSQAVGAVLSLLLVALTCCLLALLYKKERRETVISKLTTC  
 CRRSSNVSYKYSKVNKEEETDENETEWLMEEIQLPPPRQGKEGQENGHITTKSVKALS  
 SLHGDDQDSEDEVLTIP EVKVHSGRGAGAESSHPVRNAQSNALQEREDDRVGLVRGE  
 KARKGKSSSAQQKTVSSTKLVSFHDDSDDLLHI

SEQID No:243

MSDKMSSFLHIGDICS LYAEGSTNGFISTLGLVDDRCVVQPETGDLNNPPKKFRDCLFK  
 LCPMNRYSAQKQFWKA AKPGANSTTDAVLLNKLHHAADLEKKQNETENRKLLGTVIQY  
 GNVIQLLHLKSNKYLT VNKRLPALLEKNAMRVTLD EAGNEGSWFYIQPFYKLRSIGDSVV  
 IGDKVVLNPVNAGQPLHASSHQLVDNPGCNEVNSVNCNTSWKIVLFMKWSDNKDDILK  
 GGDVVRLFHAEQEKFLT CDEHRKKQHVF LRTTGRQSATSATSSKALWEVEVVQHDP  
 RGGAGYWNSLFRFKHLATGHYLA AEVDPDFEEECLEFQPSVDPDQDASRSRLRNAQE  
 KMYSLVSVPEGNDISSIFELDPTTLRGGDSLVRNSYVRLRHLCNTWVHSTNIPIDKE  
 EEKPVMLKIGTSPVKEDKEAFAIVPVSPA EVRDLDFANDASKVLGSIAGKLEKGTITQNE  
 RRSVTKLLEDLVYFVTGGTNSGQDVLEVVF SKPNRERQKLMREQNILKQIFKLLQAPFT  
 DCGDGPMLRLEELGDQRHAPFRHICRLCYRVL RHSSQQDYRKNQEYIAKQFGFMQKQI  
 GYDVLAEDTITALLHNNRKLLEKHITAAEIDTFVSLVRKNREPRFLDYLSDCVSMNKSIP  
 VTQELICKAVLNPTNADILIETKLVL SRFEFEGVSSTGENALEAGEDEEEVWLFWRDSNK  
 EIRSKSVRELAQDAKEGQKEDRDVLSYYRYQLNLFARMCLDRQYLAIN EISGQLDVLIL  
 RCMSDENLPYDLRASFCRLMLHMHVDRDPQE QVTPVKYARLWSEIPSEIAIDDYDSSG  
 ASKDEIKERFAQTMEFVEEYLRDVVCQRFPFSDKEKNKLT FEVVNLARNLIYFGFYNFS  
 DLLRLTKILLAILDCVHVTTIFPISKMAKGEENKGNNDVEKLKSSNVMRSIHGVGELMTQV  
 VLRGGGFLPMT PMAAPEGNVKQAEPEKEDIMVMDTKLKIIELQFILNVRLDYRISCLLCI  
 FKREFDESNSQTSETSSGNSSQEGPSNVP GALDFEHIEEQAEGIFGGSEENTPLDLD  
 HGGRTFLRVLLH LTMHDYPPLVSGALQLLFRHFSQRQEVLQAFKQVQLLVTSQDVDNY  
 KQIKQDLQDQRSIVEKSELWVYKGQGPDETMDGASGENEHKKTEEGNNKPQKHESTS  
 SYNRYRVKEILIRLSKLCVQESASVRKSRKQQQRLLRNMG AHAVVLELLQIPYEKAEDTK  
 MQEIMRLAHEFLQNFCAGNQQNQALLHKHINLFLNPGILEAVTMQHIFMNNFQLCSEINE

RVVQHFVHICIETHGRNVQYIKFLQTIVKAEGKFIKKCQDMVMAELVNSGEDVLVIFYNDR  
 ASFQTLIQMMRSEDRMDENSPLMYHIHLVELLAVCTEGKNVYTEIKCNSLLPLDDIVRV  
 VTHEDCIPEVKIAYINFLNH CYVDTEVEMKEIYTSNHMWKLFENFLVDICRACNNTSDRK  
 HADSILEKYVTEIVMSIVTTFFSSPFSDQSTTLQTRQPVFVQLLQGVFRVYHCNWLMP  
 QKASVESCIRVLSVAKSRAIAIPVDLDSQVNNLFLKSHSIVQKTAMNWRLSARNAARR  
 DSVLAASRDYRNIIERLQDIVSALEDRLRPLVQAELSVLVDVLHRPELLFPENTDARRKC  
 ESGGFICKLIKHTKQILLEENEEKLCIKVLQTLREMMTKDRGYGEKLISIDELDNAELPPAP  
 DSENSTEELEPSPPLRQLEDHKRGEALRQVLVNRYYGNNVRPSGRRESLTSFGNGPLSA  
 GGP GKPGGGGGGGSGSSSMSRGEMSLAEVQCHLDKEGASNLVIDLIMNASSDRVFHES  
 ILLAIALLEGGNTTIQHSFFCRLTEDKKSEKFFKVFYDRMKVAQQEIKATVTVNTSDLGNK  
 KKDDEVDRDAPSRKKAKEPTTQITEEVRDQILLEASAATRKAFITFRREADPDDHYQPG  
 EGTQATADKAKDDLEMSAVITIMQPILRFLQLLCENHNRLQNLFLRCQNNKNTNYNLVCE  
 TLQFLDCICGSTTGGLGLLGLYINEKNVALINQTLLESLTEYCQGPCHENQNCIATHESNGI  
 DIITALILNDINPLGKKRMDLVLELKNNASKLLLAIMESRHDSENAERILYNMRPKELVEVI  
 KKAYMQGEVEFEDGENGEDGAASPRNVGHNIYILAHQLARHNKELQSMMLKPGGQVDG  
 DEALEFYAKHTAQIEIVRLDRTMEQIVFPVPSICEFLTKEKSLRIYYTTERDEQGSKINDFF  
 LRSEDLFNEMNWQKKLRAQPVLYWCARNMSFWSSISFNLAVLMNLLVAFFYPFKGVR  
 GGTLEPHWSGLLWTAMLISLAIVIALPKPHGIRALIASTILRLIFSVGLQPTLFLLGAFNVCN  
 KIIFLMSFVGNCGTFTRGYRAMVLDVEFLYHLLYLVICAMGLFVHEFFYSLLLFDLVYREE  
 TLLNVIKSVTRNGRSIILTAVLALILVYLF SIVGYLFFKDDFILEVDRLPNETAVPETGESLA  
 SEFLFSDVCRVESGENCSPAPREELVPAEETE QDKEHTCETLLMCIVTVLSHGLRSGG  
 GVGDLVRKPSKEEPLFAARVIYDLLFFFMVIIIIVNLIFGVIIDTFADLRSEKQKKEEILKTTC  
 FIGGLERDKFDNKTVTFEEHIKEEHNMMWHYLCFIVLVKVKDSTEYTGPE SYVAEMIKERN  
 LDWFPRMRAMSLVSSDSEGEQNELRNLQEKLESTMKLVTNLSGQLSELKDQMTEQRK  
 QKQRIGLLGHPPHMNVNPQQPA

SEQID No:244

GGRQRCQRGRSCGAREEEVEPGTARPPPAASAMDASLEKIADPTLAEMGKNLKEAVK  
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 NIGEQQGHMALLGHSLGAYISTLDKEKLRKLTTRILSDTTWLRCRIFRYENG CAYFHEEER  
 EGLAKICRLAIHSRYEDFVVDGFNVLYNKKPVIYLSAAARPGLGQYLCNQLGLPFPCLCR  
 VPCNTVFGSQHQMDVAFLEKLIKDDIERGRLPLLLVANAGTAAVGHTDKIGRLKELCEQ  
 YGIWLHVEGVNLTALALGYVSSSVLAAAKCDSMTMTPGPWLGLPAVPAVTLYKHDDPA  
 LTLVAGLTSNKPTDKLRALPLWLSLQYLGLDGFVERIKHACQLSQRLQESLKKVNYIKILV

EDELSSPVVFRFFQELPGSDPVFKAVPVPNMTPSGVGRERHSCDALNRWLGEQLKQ  
 LVPASGLTVMLEAEGTCLRFSPLMTAAVLGTRGEDVDQLVACIESKLPVLCCTLQLRE  
 EFKQEVEATAGLLYVDDPNWSGIGVVRYEHANDDKSSLKSDPEGENIHAGLLKKLNELE  
 SDLTFKIGPEYKSMKSCLYVGMASDNVDAELVETIAATAREIEENSRLLENMTEVVVRKG  
 IQEAQVELQKASEERLLEEGVLRQIPVVGSVLWNFSPVQALQKGRTFNLTAGSLESTEPI  
 YVYKAQGAGVTLPPTPSGSRTKQRLPGQKPKFRSLRGSDALSETSSVSHIEDLEKVERL  
 SSGPEQITLEASSTEGHPGAPSPQHTDQTEAFQKGVPHPEDDHSQVEGPESLR

SEQID No:245

EPCALTPGPSHLALTFLPSKPGARPQPEGASWDAGPGGAPSAWADPGEGGPSPMLLP  
 EGLSSQALSTEAPLPATLEPRIVMGEETCQALLSPRAARTALRDQEGGHASPDPPPELC  
 SQGDLSVPSPPPDPDSFFTPPTPTKTTYALLPACGPHGDARDSEAELRDELLDSPPAS  
 PSGSYITADGDSWASSPSCSLSLAPAEGLDFPSGWGLSPQGSMVDERELHPAGTPE  
 PPSSESSLADSSSSWGQEGHFFDLDFLANDPMIPAALLPFQGSILFQVEAVEVTPLSP  
 EEEEEEAADPDPGGDLAGEGEEDSTSASFLQSLSDLSITEGMDEAFARDDTSAASS  
 DSDSASYAEADDERLYSGEPHAQATLLQDSVQKTEESGGGAKGLQAQDGTVSWAVE  
 AAPQTS DRGAYLSQRQELISEVTEEG LALGQESTATVTPHTLQVAPGLQVEVATRVTPQ  
 AGEETDSTAGQESAAMAMPQPSQEGISEILGQESVTAEKLPTPQEETSLTLCPDSPQ  
 NLKEEGGLDLPSGRKPVAAATIVPRQAKEDLTLPQDSAMTPPLPLQDSDLSSAPKPVAA  
 ATIVSQQAE EGLTLPQDSVMTPPLPLQDTELSSAPKPVAAATLV SQQAE EGLTLPQDSA  
 MTPPLPLQDSDLSSAPKPVAAATLV SQQAE EGLTLPQDSAMTPPLPLQDSDLSSAPKPV  
 AAATLV SQQAE EGLTLPQDSAMTPPLPLQDSDLSSAPKPVAAATIVSQQAE EGLTLPQD  
 SAMTPPLPLQDSDLSSAPKPVAAATIVSQQAE EGLTLPQDSAMTPPLPLQDSDLSSAPK  
 PVAAATPV SQQAE EGLTLPQDSAMTPPLPLQDSDLSSAPKPVAAATPV SQQAE EGLTL  
 PQDSAMTAPLPLQDTGPTSGPEPLAVATPQTLQAEAGCAPGTEPVATMAQQEVEGEAL  
 GPRPAPEEKNAALPTVPEPAALDQVQQDDPQPAAEAGTPWAAQEDADSTLGMEALSL  
 PEPASGAGEEIAEALSRPGREACLEARAHTGDGAKPDSPQKETLEVENQQEGGLKLLA  
 QEHGPRSALGGAREVPDAPPAACEVVSQARLLSPAREERGLSGKSTPEPTLPSAVATE  
 ASLDSCPESSVGAVSSLDRGCPDAPAPTSAPTSQQPEPVLGLGSVEQPHEVPSVLGTP  
 LLQPPENLAKGQPSTPVDRPLGPDPSAPGTLAGAALPPLEPPAPCLCQDPQEDSVEDE  
 EPPGSLGLPPPQAGVQPA AAAVSGTTQPLGTGPRVSLSPHSPLLSPKVASMDAKDLAL  
 QILPPCQVPPPSGPQSPAGPQGLSAPEQQEDED SLEEDSPRALGSGQHSDSHGESSA  
 ELDEQDILAPQTVQCPAQAPAGGSEETIAKAKQSRSEKKARKAMSKLGLRQIQGVTRITI  
 QKSKNILFVIAKPDVFKSPASDTYVVFGEAKIEDLSQQVHKAAAEKFKVPSEPSALVPES

APRPRVRLECKEEEEEEEEVDEAGLELRDIELVMAQANVSRAKAVRALRDNHSDIVNA  
IMELTM

SEQID No:246

MLTTLKPFGSVSVESKMNNKAGSFFWNLRQFSTLVSTSRTMRLCCLGLCKPKIVHSNW  
NILNNFHNRMQSTDIIRYLFQDAFIFKSDVGFQTKGISTLTALRIERLLYAKRFFDSKQSL  
VPVDKSDDELKKVNLNHEVSNEVDLTKETKPNRISSRKLSEECNSLSDVLDAFSKAPTF  
PSSNYFTAMWTIAKRLSDDQKRFEKRLMFSPAFNQLCEHMMREAKIMQYKYLLFSLH  
AIVKLGIPQNTILVQTLLRVTQERINECDEICLSVLSTVLEAMEPCKNVHVLRTGFRILVDQ  
QVWKIEDVFTLQVVMKCIGKDAPIALKRKLEMKALRELD RFSVLNSQHMFEVLAAMNHR  
SLILLDECSKVVDNIHGCP LRIMINILQSCCKDLQYHNLDL FKGGLADYVAATFDIWKFRKVL  
FILILFENLGFRPVGLMDL FMKRIVEDPESLNMKNILSILHTYSSLNHVYKCQNKEQFVEV  
MASALTGYLHTISSENLLDAVYSFCLMNYFPLAPFNQLLQKDIISELLTSDDMKNAYKLHT  
LDTCLKLDDTVYLRDIALSLPQLPRELPSSHTNAKVAEVLSSLLGGEGHFSKDVHLPHNY  
HIDFEIRMDTNRNQVLPLSDVDTTSATDIQRLLTYISFAGLSELKS

SEQID No:247

LQLSVKMSVLISQSVINYVEEENIPALKALLEKCKDVDERNECGQTPLMIAAEQGNLEIVK  
ELIKNGANCNLEDLDNWTALISASKEGHVHIVEELLKCGVNLEHRDMGGWTALMWACY  
KGRTDVVELLLSHGANPSVTGLYSVYPIIWAAGRGHADIVHLLLQNGAKVNCSDKYGTT  
PLVWAARKGHLECVKHLLAMGADV DQEGANSMTALIVAVKGGYTQSVKEILKRNP NVN  
LTDKDGNTALMIASKEGHTEIVQDLLDAGTYVNIPDRSGDTVIGAVRGGHVEIVRALLQ  
KYADIDIRGQDNKTALYWAVEKGNATMVRDILQCNPDTEICTKDGETPLIKATKMRNIEV  
VELLLDKGAKVSAVDKKGDTPLHIAIRGRSRKLAELLRNPKDGRLLYRPNKAGETPYNI  
DCSHQKSILTQIFGARHLSPTETDGDMLGYDLYSSALADILSEPTMQPPICVGLYAQWG  
SGKSFLLKKLEDEMKT FAGQQIEPLFQFSWLIVFLTLLLCGGLGLLFAFTVHPNLGIAVSL  
SFLALLYIFFIVIYFGGRREGESWNWAWVLSTRLARHIGYLELLLLKLMFVNPPPELPEQTTK  
ALPVRFLFTDYNRLSSVGGETSLAEMIATLSDACEREFGLATRLFRVFKTEDTQGGKKK  
WKKTCCLPSFVIFLFIIGCIISGITLLAIFRVDPKHLTVNAVLISIASVVGLAFVLNCRTWWQ  
VLDSLLNSQRKRLHNAASKLHKLKSEGFMKVLKCEVELMARMAKTIDSFTQNQTRLVVII  
DGLDACEQDKVLQMLD TVRVLFSGKPFIAIFASDPHIIKAINQNLNSVLRDSNINGHDYM  
RNIVHLPVFLNSRGLSNARKFLVTSATNGDVPCSDTTGIQEDADRRVSQNSLGEMTKLG  
SKTALNRRD TYRRRQMQR TITRQMSFDLTKLLVTEDWFSDISPQTMRRLLNIVSVTGRL  
LRANQISFNWDR LASWINLTEQWPYRTSWLILYLEETEGIPDQMTLKTIERISKNIPTTK

DVEPLLEIDGDIRNFEVFLSSRTPVLVARDVKVFLPCTVNLDPKLREIIADVRAAREQISIG  
 GLAYPPLPLHEGPPRAPSGYSQPPSVCSSTSFNPGPFAGGVVSPQPHSSYYSGMTGPQ  
 HPFYNRPFAPYLYTPRYYPGGSQHLISRPSVKTS�PRDQNNGLEVIKEDAAEGLSSPT  
 DSSRGSGPAPGPVLLNSLNVDACEKQIEGLDQSMPLQYCTTIKKANINGRVLAQC  
 NIDELKKEMNMNFGDWHLFRSTVLEMRNAESHVVPEDPRFLSESSSGPAPHGEPARR  
 ASHNELPHTELSSQTPYTLNFSFEELNTLGLDEGAPRHSNLSWQSQTRRTPSLSSLNS  
 QDSSIEISKLTDKVQAEYRDAYREYIAQMSQLEGPGSTTISGRSSPHSTYYMGQSSSG  
 GSIHSNLEQEKGKDSEPKPDDGRKSFLMKRGDVIDYSSSGVSTNDASPLDPITEEDEKS  
 DQSGSKLLPGKKSSERSSLFQTDLKKGSGRLRYQKLPSDEDESGTEESDNTPLLKDDK  
 DRKAEGKVERVPKSPEHSAEPIRTFIKAKEYLSDALDKKDSSDSGVRSSSESSPNHSLH  
 NEVADDSQLKANLIELEDDSHSGKRGIPHSLSGLQDPPIARMSICSEDKKSPSECSLIAS  
 SPEENWPACQKAYNLNRTPTSTVTLNNNSAPANRANQNFDEMEGIRETSQVILRPSSSP  
 NPTTIQENENLKSMTHKRSQRSSYTRLKDPPELHAAASSESTGFGEEERESIL

SEQID No:248

MEAAPPGPWPLLLLLLLLLALCGCPAPAAASPLLLFANRRDVRLVDAGGVKLESTIVVS  
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 GKPLYWTDSETNRIEVANLNGTSRKVLFWQDLQDPRAIALDPAHGYMYWTDWGETPRI  
 ERAGMDGSTRKIIVDSDIYWPNGLTIDLEEQLYWADAKLSFIHRANLDGSFRQKVVEG  
 SLTHPFALTLSGDTLYWTDWQTRSIHACNKRTGGKRKEILSALYSPMDIQVLSQERQPF  
 FHTRCEEDNGGCSHLCLLSPSEPFYTCACPTGVQLQDNGRTCKAGAEVLLARRTDL  
 RRISLDTPDFTDIVLQVDDIRHAIADYDPLEGYVYWTDDEVRAIRRAYLDGSGAQTIVNT  
 EINDPDGIAVDWVARNLYWTDGTGTDRIEVTRLNGTSRKILVSEDLDPEPRAIALHPVMGLM  
 YWTDWGENPKIECANLDGQERRVLVNASLGWPNGLALDLQEGKLYWGDAKTDKIEVIN  
 VDGTKRRTLLEDKLPHFIFGFTLLGDFIYWTDWQRRSIERVHKVKASRDVIIDQLPDLMGL  
 KAVNVAKVVGTPNPCADRNGGCSHLCCFTPHATRCGCPIGLELLSDMKTCIVPEAFVFT  
 SRAAIHRISLETNNNDVAIPLTGVKEASALDFDVSNNHIYWTDVSLKTISRFRMNGSSVE  
 HVVEFGLDYPEGMAVDWMGKNLYWADTGTNRIEVARLDGQFRQVLVWRDLNPRSL  
 ALDPTKGYIYWTEWGGKPRIVRAFMDGTNCMTLVDKVGRANDLTIDYADQRLYWTDLD  
 TNMIESSNMLGQERVVIADDLPHPFGLTQYSDIYWTDWNLHSIERADKTSGRNRTLQ  
 GHLDVFMDILVFHSSRQDGLNDCMHNNQCGQLCLAIPGGHRCGCASHYTLPSSRN  
 CSPPTTFLFSQKSAISRMIPDDQHSPDLILPLHGLRNVKAIDYDPLDKFIYWVDGRQNIK  
 RAKDDGTQPFVLTSLSQGQNPDRQPHDLSIDIYSRTLFWTCEATNTINVHRLSGEAMGV  
 VLRGDRDKPRAIVVNAERGYLYFTNMQDRAAKIERAALDGTEREVLTFTGLIRPVALVD



NTLGKLFWVDADLKRIESCDLSGANRLTLEDANIVQPLGLTILGKHLYWIDRQQQMIE  
 EKTGDKRTRIQQGRVAHLTGIIHAVEEVSLIEFSAHPCARDNNGGCSHICIAKGDGTPRCS  
 CPVHLVLLQNLLTCGEPPTCSPDQFACATGEIDCIPGAWRCDGFPECDDQSDEEGCPV  
 CSAAQFPCARGQCVDLRLRCDGEADCQDRSDEVDCDAICLPNQFRCASGQCVLKQQ  
 CDSFPDCIDGSDELMCEITKPPSDDSPAHSAGPVGIIILSLFVMGGVYFVCQRRVVCQR  
 YAGANGPFPHEYVSGTPHVPLNFIAPGGSQHGPFTHGACGKSMSSVSLMGGRGGVP  
 LYDRNHVTGASSSSSSSTKATLYPPILNPPSPATDPSLYNMDMFYSSNIPATARPYP  
 YIIRGMAPPPTTPCSTDVCDSDYSASRWKASKYYLDLNSDSDPYPPPTPHSQYLSAEDS  
 CPPSPATERSYFHLFPPPPSPCTDSS

SEQID No:249

MDMFPLTWVFLALYFSRHQVRGQPDPPCGGRLNSKDAGYITSPGYPDYPSHQNCE  
 WIVYAPEPNQKIVLNFNPHFEIEKHCKYDFIEIRDGDSEADLLGKHCGNIAPPTIISGS  
 MLYIKFTSDYARQGAGFSLRYEIKTGSEDCSKNFTSPNGTIESPGFPEKYPHNLDCTFT  
 ILAKPKMEIILQFLIFDLEHDPLQVGECDCKYDWLDIWDGIPHVGPLIGKYCGTKTPSEL  
 SSTGILSLTFHTDMAVAKDGFSARYLVHQEPLNFQCNVPLGMESGRIANEQISASST  
 YSDGRWTPQQSRLHGDDNGWTPNLDNKEYLQVDLRLTMTLTAIATQGAISRETQNG  
 YYVKSYSKLEVSTNGEDWMVYRHGKNHKVFQANNDATEVVLNKLHAPLLTRFVRIRPQT  
 WHSGIALRLELFGCRVTDAPCSNMLGMLSLGLIADSQISASSTQEYLWSPSAARLVSSRS  
 GWFPRIPQAQPGEEWLQVDLGTPTVKGVIIQGARGGDSITAVEARAFVRKFKVSYSLN  
 GKDWEYIQDPRTQQPKLFEGNMHYDTPDIRRFDPIPAQYVRVYPERWSPAGIGMRLEV  
 LGCDWTDKPTVETLGPTVKSEETTPYPTEEEATECGENCSSFEDDKDLQLPSGFNCN  
 FDFLEEPCGWMYDHAKWLRTTWASSSSPNDRTPDDRNLRLQSDSQREGQYARLIS  
 PPVHLPRSPVCMFQYQATGGRGVALQVVREASQESKLLWVIREDDQGGGEWKHGRIILP  
 SYDMEYQIVFEGVIGKGRSGEIAIDDIRISTDVPLENCMEPISAFAGENFKVDIPEIHEREG  
 YEDEIDDEYEVDWSNSSSATSGSGAPSTDKEKSWLYTLDPILITIIAMSSLGVLGATCA  
 GLLLYCTCSYSGLSSRSCTTLENYNFELYDGLKHKVKMNHQKCCSEA

SEQID No:250

MVSRCSCLGVQCCLLLSLLLLAAWEVGSGLHYSVYEEARHGTFVGRIAQDLGLELAELV  
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 VEVKDINDNPPRFVTEQKLSIPESRLLDSPFLEGASDADVGENALLTYKLSPNEYFVL  
 DIINKKDKDKFPVLVLRKLLDREENPQLKLLLTATDGGKPEFTGSVSLILVLDANDNAPIF  
 DRPVYEVKMYENQVNQTLVIRLNASDSDEGINKEMMYSFSSLVPPTIRRKFWINERTGEI

KVND AIDFEDSNTYEIHVDVTDKGNPPMVGHCTVLVELLDENDNSPEVIVTSLSLPVKED  
 AQVGT VIALISVSDHDSGANGQVTC SLTPHVPFKLVSTYKNYYSLV LDSALDRERV SAY  
 ELVVTARDGGSPPLWATASVSVEVADVNDNAPAF AQSEYTVFVKENNPPGCHIFTVSA  
 WDADAQENALVSYS LVERRLGERSLSSYVSVHAESGKVYALQPLDHEELELLQFQVSA  
 RDGGVPPLG SNLT LQVFVLDENDNAPALLASPAGSAGGAVSELVLR SVVAGHV VAKVR  
 AVDADSGYN AWLSYELQSAAVGARIPFRVGLYTGEISTTRALDETDSPRQRLLVLVKDH  
 GEPSLTATATVLVSLVEGSQAPKASSRASVGV APEVALVDVNVYLI ICAVSSLLVLTLL  
 YTALRCSAAPTEGACGPVKPTLVCS SAVGSWSYSQQRRQRVCSGEGLPKADLMAFSP  
 SLPPCPMVDVDGEDQSIGGDHSRKPRQPNPDWRY SASLRAGMHSSVHLEEAGILRAG  
 PGGPDQQWPTVSSATPEPEAGEVSP PVGAGVNSNSWTFKYGPGNPKQSGPGELPK  
 FIIPGSPA IISIRQEPTNSQIDKSDFITFGKKEETKKKKKKKKGNKTQEKKEKGNSTTDNSD  
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SEQID No:251

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 LQIELQVRDINDHSPVFLEKEMLLEIPENSPVGAVFLLES AKDLVDGINAVKSYTINPN SH  
 FHVKIRVNP DN RKYPELVLDKALDY EERPELSFILTALDGGSPPRSGTALVRVVVDIND  
 NSPEFEQAFYE VKILENSILGSLVVTVSAWDLDSGTNSELSYTFSHASEDIRKTFEINQKS  
 GDITLTAPLDFEAI ESYSIIIQATDGGGLFGKSTVRIQVMDVNDNAPEITVSSITSPIENTP  
 ETVVMVFRIRDRDSGDNGKMVCSIPEDIPFVLKSSVNYYTLETERPLDRESRAEYNITI  
 TVTDLGT PRLKTEHNITVLVSDVNDNAPAF TQTSYALFVRENNSPALHIGSISATDRDSG  
 TNAQVNYSLLPSQDPHLPLASLV SINADNGHLFALRSLDY EALQGFQFRVGATDHGSPA  
 LSSEALVRVLVLDANDNSPFVLYPLQNGSAPCTELVPWAAEPGYLVTKVVAVDGD SGQ  
 NAWLSYQLLKATEPGLFGVWAHNGEVRTARLLSERDA AKHRLVVLVKDNGEPPRSATA  
 TLHVLLVDGFSQPYLPLPEAAPAQADSLTVYLVVALASVSSLFLFSVLLFVAVRLCRR  
 SRAAPVGRC SVPEGPFPGHLVDVSGTGTLSQSYHYEVCVTGGSR SNKFKFLKPIIPNFL  
 PQSTGSEVEENPPFQNNLGF

SEQID No:252

MEASGKLICRQRQVLFSFLLLGLSLAGAAEPRSYSVVEETEGSSFVTNLAKDLGLEQRE  
 FSRRGVRVVS RGNKLHLQLNQETADLLLNEKLDREDLCGHTEPCVLR FQVLLLESPFEFF  
 QAE LQVIDINDHSPVFLDKQMLVKVSESSPPGTTFPLKNAEDLDVGQNNIENYIISPNSYF  
 RVLTRKRS DGRKYPELVLDKALDREEEAELRLTLALDGGSPPRSGTAQVYIEVLDVND

NAPEFEQPFYRVQISEDSPVGFLVVKVSATDVDTGNGEISYSLFQASEEIGKTFKINPL  
 TGEIELKKQLDFEKLQSYEVNIEARDAGTFSGKCTVLIQVIDVNDHAPEVTMSAFTSPIPE  
 NAPETVVALFSVSDLDSENGKISCSIQEDLPFLKSAENFYTLTERPLDRESRAEYNIT  
 ITVTDLGTPLITQLNMTVLIADVNDNAPAFQTQTSYTLFVRENNSPALHIRSVSATDRDSG  
 TNAQVTYSLLPPQDPHLPLTSLVSINADNGHLFALRSLDYEALQGFQFRVGASDHGSPA  
 LSSEALVRVVLDANDNSPFVLYPLQNGSAPCTELVPRAAEPGYLVTKVVAVDGDSGQ  
 NAWLSYQLLKATELGFGVWAHNGEVRTARLLSERDAAKHRLVVLVKDNGEPPRSATA  
 TLHVLLVDGFSQPYLPLPEAAPTQAQADLLTVYLVVALASVSSLFLFSVLLFVAVRLCRR  
 SRAASVGRCLVPEGPLPGHLVDMSGTRTLSQSYQYEVCLAGGSGTNEFKFLKPIIPNFP  
 PQCPGKEIQGNSTFPNNFGFNIQ

SEQID No:253

MKKLGRIHPNRQVLAFILMVFLSQVRLEPIRYSVLEETESGSFVAHLAKDLGLGIGELASR  
 SARVLSDDDKQRLQLDRQTGDLLLREKLDREELCGPIEPCVLHFQVFLEMPVQFFQGEL  
 LIQDINDHSPIFPEREVLLKILENSQPGLTFLPIAEDLDVGSNGLQKYTISPNSHFILTRN  
 HSEGKKYPDLVQDKPLDREEQPEFSLTLVALDGGSPPRSGTVMVRILIMDINDNAPEFV  
 HTPYGVQVLENSPLDSPIVRVLARDIDAGNFGSVSYGLFQASDEIKQTFSINEVTGEILLK  
 KKLDFEKIKSYHVEIATDGGGLSGKGTVVIEVDVNDNPPELISSLTSSIPENAPETVVS  
 IFRIRDRDSGENGKMICSIPDNLPFILKPTLKNFYTLVTERPLDRETSAEYNITIAVTDLGT  
 RLKTQQNITVQVSDVNDNAPAFQTQTSYTLFVRENNSPALHIGSVSATDRDSGTNAQVTY  
 SLLPPQDPHLPLASLVINADNGHLFALRSLDYEALQAFEFVRVGASDRGSPALSSEALV  
 RVLVLDTNDNSPFVLYPLQNGSAPCTELVPRAAEPGYLVTKVVAVDGDSGQNAWLSYQ  
 LLKATEPGLFGVWAHNGEVRTARLLSERDAAKHRLVVLVKDNGEPPRSATATLHVLLVD  
 GFSQPYLPLPEAAPAQQAQADSLTVYLVVALASVSSLFLFSVLLFVAVRLCRRSRAASVG  
 RCSVPEGPFPGHLVDVSGTGTLTSQSYQYEVCLTGDSGTGEFKFLKPIFPNLLVQDTGR  
 EVKENPKFRNSLVFS

SEQID No:254

MQRAREAEEMMSQVLFPFLLSLFCGAISQQIRYTIPEELANGSRVGKLAIDLGLSVREL  
 PTRKLRVSAEDYFNVSLESGDLLVNGRIDREKICGRKLECALEFETVAENPMNVFHVVV  
 VIQDINDNAPRFVAKGIDLEICESALPGVKFSLDSAQDADVEGNSLKLYTINPNQYFSLST  
 KESPDGSKYPVLLLEKPLDREHQSSHRLILTAMDGGDPPLSGTTHIWIRVTDANDNAPV  
 FSQEVYRVSLQENVPWGTSVLRVMATDQDEGINAEITYAFLNSPISTSLFNLNPNTGDIT  
 TNGTLDFEETSRYVLSVEAKDGGVHTAHCNVQIEIVDENDNAPEVTFMSFSNQIPEDSD

LGTVIALIKVRDKDSGQNGMVTCTQEEVPFKLESTSKNYYKLVIAGALNREQTADYNVT  
 IIATDKGKPALSSRTSITLHISDINDNAPVFHQASYVVHVSENNPPGASIAQVSASDPDLG  
 PNGRVSYISLASDLEPRELLSYVSVSPQSGVVFAQRAFDHEQLRAFELTLQARDQGSPA  
 LSANVSLRVLVGDLNDNAPRVLYPALGPDGSAFFDMVPRAAEPGYLVTKVVAVDADSG  
 HNAWLSYHVLQASEPGLFSLGLRTGEVRTARALGDRDAARQRLLVAVRDGGQPPLSA  
 TATLHLIFADSLQEVLPLSDRPEPSDPQTELQFYLVVALALISVLFLLAVILAIALRLRRSS  
 SLDTEGCFQTGLCSKSGPGVPPNHSEGTLPSYNLCIASHSAKTEFNSLNLTPEMAPPQ  
 DLLCDDPSMVVCASNEDHKIAYDPSLSSHQAPPNTDWRFSQAQRPGTSGSQNGDDTG  
 TWPNNQFDTEMLQAMILASASEAADGSSTLGGGAGTMGLSARYGPQFTLQHVPDYRQ  
 NVYIPGSNATLTNAAGKRDGKAPAGGNGNKKKSGKKEKK

SEQID No:255

MGGSCAQRRRAGPRQVLFPLLLPLFYPTLSEPIRYSIPEELAKGSVVGNLAKDLGLSVLD  
 VSARKLRVSAEKLHFSVDAESGDLVKNRIDREQICKERRRCELQLEAVVENPLNIFHVI  
 VVIEDVNDHAPQFDKKEIHLEIFESASAGTRLSLDPATDPDININSIKDYKINSNPYFSLMV  
 RVNSDGGKYPELSLEKLLDREEQRSHSLILTALDGGDPPRSATAHIEISVKDTNDNPPVF  
 SRDEYRISLSENLPGPSVLQVTATDQDEGVNAEINYYFRSTAQSTKHMFSLEDEKTGMI  
 KNNQSFD FEDVERYTMEVEAKDGGGLSTQCKVIIELDENDNSPEIIITSLSDQILENSPP  
 GMVVALFKTRDLDFGGNGEVRNCNIETDIPFKIYSSSNYYKLVTGDALDREQTPEYNVTI  
 VATDRGKPLSSSRISITLYVADINDNAPVFDQTSYVVHVAENNNPPGASIAQVSASDPDL  
 GLNGHISYSIVASDLEPLAVSSYVSVSAQSGVVFAQRAFDHEQLRAFALTLQARDHGSP  
 TLSANVSLRVLVGDRNDNAPRVLYPALGPDGSAFFDMVPRSAEPGYLVTKVVAVDADS  
 GHNAWLSYHVLQASEPGLFSLGLRTGEVRTARALGDRDAARQRLLVAVRDGGQPPLS  
 ATATLHLVFNADNLQEILPLSDRPVLSDPQAEQFYLVVALALISVLFLLAVILAIALRLRRS  
 LSPATWDCFHPGLCVKSGPVVPPNYSEGTLPSYNLCIAHTGTKEFNFLKCSVPLHSNE  
 DMVCSVSPGALIPPHGGEDLTSHPETLSQAPPNTDWRFSQAQRPGTSGSQNGDDTG  
 TWPNNQFDTEMLQAMILASASEAADGSSTLGGGAGTMGLSARYGPQFTLQHVPDYRQ  
 NVYIPGSNATLTNAAGKRDGKAPAGGNGNKKKSGKKEKK

SEQID No:256

MAAAAARVVLSSAARGGLWGFSESLIRGAAGRSLYFGENRLRSTQAATQVVLNVPET  
 RVTCLSEGLRVASEDSGLSTCTVGLWIDAGSRYENEKNNGTAHFLEHMAFKGTKKRSQ  
 LDLELEIENMGAHLNAYTSREQTVYYAKAFSKDLPRAVEILADIIONSTLGEAEIERERGV  
 LREMQUEVETNLQEVVFDYLHATAYQNTALGRTILGPTENIKSISRKDLVDYITTHYKGPRI

VLAAGGVSHDELLDLAKFHFGDSLCTHKGEIPALPPCKFTGSEIRVRDDKMPLAHLAIA  
 VEAVGWAHPDTICLMVANTLIGNWDRSFGGGMNLSSKLAQLTCHGNLCHSFQSFNTSY  
 TDTGLWGLYMVCESTVADMLHVQKEWMRLCTSVTESEVARARNLLKTNMLLQLDG  
 STPICEDIGRQMLCYNRRIPPELEARIDAVNAETIREVCTKYIYNRSPAIAAVGPIKQLPDF  
 KQIRSNMCWLRD

SEQID No:257

MGAYLSQPNTVKCSGDGVGAPRLPLPYGFSAMQGWRVSMEDAHNCIPELDSETAMFS  
 VYDGHGGEEVALYCAKYLPDIKDQKAYKEGKLQKALEDAFLAIDAKLTTEEVIKELAQIA  
 GRPTEDEDEKEKVADEDDVDNEEAALLHEEATMTIEELLTRYGQNCHKGPPHSKSGGG  
 TGEEPGSQGLNGEAGPEDSTRETSPSQENGPTAKAYTGFSNSERGTEAGQVGEPGIP  
 TGEAGPSCSSASDKLPRVAKSKFFEDSEDESDEAEEDDSEECSEEDDGYSSSEEAEEN  
 EEDEDDTEEAEDDEEEEEEMMVPGMGKEEPGSDSGTTAVVALIRGKQLIVANAGDS  
 RCVVSEAGKALDMSYDHKPEDEVELARIKNAGGKVTMDGRVNGGLNLSRAIGDHFYKR  
 NKNLPPEEQMISALPDIKVLTLTDDHEFMVIACDGIWNVMSSQEVVDFIQSKISQRDENG  
 ELRLLSSIVEELLQCLAPDTSGDGTGCDNMTCIICFKPRNTAELQPESGKRKLEEVLS  
 EGAEENGNSDKKKKAKRD

SEQID No:258

MMETPLPKAPEKRQVTAIIFLLLLWEAGSATIKYSVLEERDSGSFVANLAKDLGLGVGEL  
 AARGARILSKGNKQYLQLERKSGNLLLKEKLDREELCGDIDPCILHFQMLLKNPVQFIQG  
 ELQLQDVNDHAPEFLENEILLKISEGSHPGTSFPLKIAQDLVDVGSNTVQNYSISTNSYFHL  
 FTRNHSDGKKYPELVLDQALDREEQPQLRLTLTALDGGSPPRGTGSQVLIVIVDINDNVP  
 EFAQRRYEYVQVPENTPIGSLVITVSARDLDAGTHGELSYSFFQYSNQIIQAFEINSITGEIR  
 FKKALDFEEIQSYHMEVEASDGGGLSGKCTVAIEVMDINDNAPELTMSLLISDILENSPET  
 VVAVFGISDPDSGNGKMMCSIQDHLPLKPTLENFYTLTTEGALDRESRAEYNITITVT  
 DLGTPRLKTEYNITLRVSDVNDNAPAFQTQSYTLFVRENNSPALHIGSVSATDRDSGTN  
 AQVTYSLLPPQNPHLPLASLVSINTDNGHLFALRSLDYEALQEFEFVRVGASDRGSPALS  
 SEALVRVLVCWTPPTTTRPSCCTRCRTAPRPAPSWCPGRPSRATW

SEQID No:259

MLRMRTAGWARGWCLGCCLLLPLSFSLAAAKQLLRYRLAEEGPADVRIGNVASDLGIV  
 TGSGEVTFSLESGSEYLIKIDNLTGELSTSERRIDREKLPPCQMIFDENECFLDFEVSIG  
 PSQSWVDLFEGQVIVLDINDNTPTFPSPVLTLTVEENRPVGTLYLLPTATDRDFGRNGIE

RYELLQEPGGGGSGGESRRAGAADSAPYPGGGGNGASGGGSGGSKRRLDASEGGG  
 GTNPGGRSSVFELQVADTPDGEKQPQLIVKGALDREQRDSYELTLRVRDGGDPPRSS  
 QAILRVLITDVNDNSPRFEKSVYEADLAENSAPGTPIQLRAADLDVGVNGQIEYVFGAA  
 TESVRRLRLDETSGLWSVLHRIDREEVNQLRFTVMARDRGQPPKTDKATVVLNIKDEN  
 DNVPSIEIRKIGRIPLKDGVANVAEDVLVDTPIALVQVSDRDQGENGVVTCTVVGDPFQ  
 LKPASDTEGDQNKKKYFLHTSTPLDYEATREFNVVIVAVDSGSPSLSSKNSLIVKVGDTN  
 DNPPMFGQSVVEVYFPENNIPGERVATVLATDADSGKNAEIAYS LDSSVMGIFAIDPDS  
 GDILVNTVLDREQTDREYEFKVNAKDKGIPVLQGSTTVIVQVADKNDNDPKFMQDVFTFY  
 VKENLQPNSPVGMVTVMDADKGRNAEMSLYIEENNNIFSIENTGTIYSTMSFDREHQT  
 TYTFRVKAVDGGDPPRSATATVSLFVMDENDNAPT VTL PKNISY TLLPPSSNVRTVVAT  
 VLATDSDDGINADLNYSIVGGNPFKLFEIDPTSGVVSLVGKLTQKH YGLHRLVVQVND S  
 GQPSQSTTTVVHVFNESVSNATAIDSQIARSLHIPLTQDIAGDPSYEISKQRLSIVIGVVA  
 GIMTVILILIVVMARYCRSKNKNNGYEAGKKDHEDFFTPQQHDKSKKPKKDKKNKSKQP  
 LYSSIVTVEASKPNGQRYDSVNEKLSDSPSMGRYRSVNGGPGSPDLARHYKSSSPLPT  
 VQLHPQSPTAGKKHQAVQDLPPANTFVGAGDNISIGSDHCSEYSCQTNNKYSKQMR LH  
 PYITVFG

SEQID No:260

MEIGWMHNRRQRQVLVFFVLLSLSGAGAE LGSYSVVEETERGSFVANLGKDLGLGLTE  
 MSTRKARIISQGNKQHLQLKAQTGDLLINEKLDREELCGPTEPCILHFQVLMENPLEIFQ  
 AELRVIDINDHSPMFTEKEMILKIPENSPLGTEFPLNHALDLVDG SNNVQNYKISPSSHFR  
 VLIHEFRDGRKYPELVLDKELDREEEPQLRLTLTALDGGSPPRSGTAQVRIEVDINDNA  
 PEFEQPIYKVQIPENSPLGSLVATVSARDLDGGANGKISYTLFQPS EDISKTLEVNPMTG  
 EVRLRKQVDFEMVTSYEVRIKATDGGGLSGKCTLLLQVVDVNDNPPQVTMSALTPIPE  
 NSPEIVVAVFSVSDPD SGNNGKTISSIQEDLPFLKPSVKNFYTLVTERALDREARAEYNI  
 TLTVTDMGTPRLKTEHNITVQISDVNDNAPTFTQTSYTLFVRENNSPALHIGSVSATDRD  
 SGTNAQVTYSLLPPQDPHLPLASLV SINADNGHLFALRSLDYEALQAFEF RVGATDRGS  
 PALSREALVRVLVLDANDNSPFVLYPLQNGSAPCTELVPRAAEPGYLVTKVVAVDGDS  
 GQNAWLSYQLLKATEPGLFGVWAHNGEVRTARLLSERDAAKQRLVVLVKDNGEPPRS  
 ATATLHVLLVDGFSQPFLPLPEAAPGQTQANSLTVYLVVALASVSSLFLFSVLLFVAVRL  
 CRRSRAASVGRCSMPEGPFPGRLVDVSGTGTLSQSYQYEVCLTGGSETSEFKFLKPIIP  
 NFSP

## SEQID No:261

MDEDVLTTLKILIIGESGVGKSSLLLRFTDDTFDELAATIGVDFKVKTISVDGNKAKLAIW  
DTAGQERFRTLTPSYRGAQGVLVYDVTRRDTFVKLDNWLNELETYCTRNDIVNMLVG  
NKIDKENREVDREGLKFARKHSMLFIEASAKTCDGVQCAFEELVEKIIQTPGLWESEN  
QNKGVKLSHREEGQGGGACGGYCSVL

## SEQID No:262

MESRDHNNPQEGPTSSSGRRRAVEDNHLLIKAVQNEDVDLVQQLLEGGANVNFQEEE  
GGWTPHNAVQMSREDIVELLRRHGADPVLRRKNGATPFILAAIAGSVKLLKLFLSKGAD  
VNECDFYGFATFMEAAVYGKVKALKFLYKRGANVNLRRKTKEDQERLRKGGATALMDA  
AEKGHVEVLKILLDEMGADVNAACDNMGRNALIHALLSSDDSDVEAITHLLLDHGADVNV  
RGERGKTPLILAVEKKHLGLVQRLLQEHEIINDTSDGKTALLLAVELKLKKIAELLCKR  
GASTDCGDLVMTARRNYDHSVLKVLLSHGAKEDFHPPAEDWKPQSSHWGAALKDLHR  
IYRPMIGKLKFFIDEKYKIADTSEGGIYLGIFYEKQEVAVKTFCEGSPRAQREVSCLOSSR  
ENSHLVTFYGSSESHRGHLFVCVTLCEQTLEACLDVHRGEDVENEDEFARNVLSSIFKA  
VQELHLSCGYTHQDLQPQNILIDSKKAAHLADFDKSIKWAGDPQEVKRDLEDLGRVLVLY  
VVKKGSISFEDLKAQSNEEVVQLSPDEETKDILHRLFHPGEHVRDCLSDLLGHPFFWTW  
ESRYRTLNRVGNESDIKTRKSESEILRLLQPGPSEHSKSFDKWTTKINECVMKKMNKFY  
EKRGNFYQNTVGDLLKFIRNLGEHIDEEEKHKMKMLKIGDPSLYFQKTFPDLVIYVYTKLQ  
NTEYRKHFPPQTHSPNKPQCDGAGGASGLASPGC

## SEQID No:263

MACSIVQFCYFQDLQAARDFLFPHLREEILSGALRRDPSKSTDWEDDGWGAWEENEP  
QEPEEEGNTCKTQKTSWLQDCVLSLSPTNDLMVIAREQKAVFLVPKWKYSDKGKEEM  
QFAVGWWSGLNVEEGECVTSALCIPLASQKRSSTGRPDWTCIVVGFTSGYVRFYTENG  
VLLLAQLLNEDPVLQLKCRTYEIPRHPGVTEQNEELSILYPAAIVTIDGFSLFQSLRACRN  
QVAKAAASGNENIQPPPLAYKKWGLQDIDTIIDHASVGIMTLSPFDQMKTASNIGGFNAA  
IKNSPPAMSQYITVGSNPFTGFFYALEGSTQPLLSHVALAVASKLTSALFNAASGWLGW  
KSKHEEEAVQKQKPKVEPATPLAVRFGPLDSRRHGESICLSPCNTLAAVTDDFGRVILL  
DVARGIAIRMWKGYRDAQIGWIQTVEDLHERVPEKADFSPFGNSQGSPSRVAQFLVIYAP  
RRGILEVWSTQQGPRVGAFNVGKHCRLLYPGYKIMGLNNVTSQSWQPQTYQICLVDPV  
SGSVKTVNVPFHLALSDKKSERAKDMHLVKKLAALLKTKSPNLDLVETEIKELIDIKYPA  
TKKQALESILASERLPFSCLRNTQTLMDTLKSQELESVDEGLLQFCANKLKLQLYESVS  
QLNSLDFHLDTPFSDNDLALLRLDEKELLKLQALLEKYKQENTRTNVRFSDDKDGVL

VKTFLEYLEYEKDVLNIKKISEEEYVALGSFFFWKCLHGESSTEDMCHTLESAGLSPQLL  
 LSLLSVWLSKEKDILDKPQSICCLHTMLSLLSKMKVAIDETWDSQSVSPWWQQMRTA  
 CIQSENNGAALLSAHVGHSAQAISNNMTEKKFSQTVLGADSEALTDSEALSOLDTEY  
 WKLLLKQLEDCLILQTLLHSGKNTQTSKVSSLQAEPLPRLSVKKLLEGGKGGIADSVAK  
 WIFKQDFSPEVLKLANEERDAENPDEPKEGVNRSFLEVSEMEMDLGAIPDLLHLAYEQF  
 PCSLELDVLHAHCCWEYVQWNKDPEEARFFVRSIEHLKQIFNAHVQNGIALMMWNTF  
 LVKRFSAAATYLMKVKGSPKDRLCRRDVGMSDTAMTSFLGSCDLLQILMEADVSRDEI  
 QVPVLDTEDAWLSVEGPISIVELALEQKHIHYPLVEHHSILCSILYAVMRFSLKTVPKPLSLF  
 DSKGKNAFFKDLTSIQLLPSGEMDPNFISVRQQFLLKVVSAAVQAQHSATKVKDPTEEA  
 TPTPGKDQDWPALAVDLAHLQVSEDVRRHYVGELYNYGVDHLGEEAILQVHDKEV  
 LASQLLVLTGQRLAHALLHTQTKEGMELLARLPPTLCTWLKAMDPODLQNTVEPIATTA  
 KLVNKVIELLPEKHGQYGLALHLIEAVEAISLPSL

SEQID No:264

MTVSGPGTPEPRPATPGASSVEQLRKEGNELFKCGDYGGALAAAYTQALGLDATPQDQ  
 AVLHRNRAACHLKLEDYDKAETEASKAIEKDGGDVKALYRRSQALEKLGRLDQAVLDLQ  
 RCVSLEPKNKVFQEALRNIGGQIQEKVRYMSSTDAKVEQMFQILLDPEEKGTEKKQKAS  
 QNLVVLAREDAGAEEKIFRSNGVQLLQRLDMGETDLMLAALRTLVGICSEHQSRVATL  
 SILGTRRVVSILGVESQAVSLAACHLLQVMFDALKEGVKKGFRGKEGAIIVDPARELKVLI  
 SNLLDLLTEVGVSGQGRDNALTLLIKAVPRKSLKDPNNSLTLWVIDQGLKKILEVGGSLQ  
 DPPGELAVTANSRMSASILLSKLFDDLKCDARENFHRLCENYIKSWFEGQGLAGKLRA  
 IQTVSCLLQGPCDAGNRALELSGVMESVIALCASEQEEELVAVEALIHAAGKAKRASFI  
 TANGVSLLKDLYKCSEKDSIRIRALVGLCKLGSAGGTDFSMKQFAEGSTLKLAKQCRKW  
 LCNDQIDAGTRRWAVEGLAYLTFDADVKEEFVEDAAALKALFQLSRLEERSVLF AVASA  
 LVNCTNSYDYEEPDPKMVELAKYAKQHVPEQHPKDKPSFVRARVKLLAAGVVSAMVC  
 MVKTESPVLTSRELLSRVFLALVEEVEDRGTVAQGGGRALIPLALEGTDVGQTKAA  
 QALAKLTITSNPEMTFPGERIYEVVRPLVSLHLNCSGLQNFEALMALTNLAGISERLRQ  
 KILKEKAVPMIEGYMFEEHEMIRRAATECMCNLAMSKEVQDLFEAQGNDRLLKLLVLYSG  
 EDELLQRAAAGGLAMLTSMRPTLCSRIQVTTTHWLEILQALLSSNQELQHRGAVVVL  
 NMVEASREIASTLMESEMMEILSVLAKGDHSPVTRAAAACLDKAVEYGLIQPNQDGE

SEQID No:265

MRPEPGGCCCRRTVRANGCVANGEVRNGYVRSSAAAAAAAAAAGQIHHTQNGGLYK  
 RPFNEAFEETPMLVAVLTYVGYGVLTFLGYLRDFLRYWRIEKCHHATEREEQKDFVSLY



QDFENFYTRNLYMRIRDNWNRPICSVPGARVDIMERQSHDYNWSFKYTGNIIKGVINMG  
 SYNLYGFARNTGSCQEAAAKVLEEYGAGVCSTRQEIGNLDKHEELEELVARFLGVEAA  
 MAYGMGFATNSMNIPALVGKGCLILSDELNHASLVLGARLSGATIRIFKHNNMQSLEKLL  
 KDAIVYGQPRTRRPWKKILILVEGIYSMEGSIVRLPEVIALKKKYKAYLYLDEAHSIGALGP  
 TGRGVVEYFGLDPEDVDVMMGTFTKSFGASGGYIGGKKELIDYLRTHSHSAVYATSLS  
 PPVVEQIITSMKCIMGQDGTSLGKECVQQLAENTRYFRRRLKEMGFIYGNEDSPVVPL  
 MLYMPAKIGAFGREMLKRNIGVVVVGFPATPIESRARFCLSAAHTKEILD TALKEIDEVG  
 DLLQLKYSRHRLVPLLD RPFDETTYEETED

SEQID No:266

MSGELPPNINIKEPRWDQSTFIGRANHFFTVDPRNILLTNEQLESARKIVHDYRQGIVP  
 PGLTENELWRAKYIYDSAFHPDTGEKMILIGRMSAQVPMNMTITGCMMTFYRTTPAVLF  
 WQWINQSFNAAVNYTNRSGDAPLTVNELGTAYVSATTGAVATALGLNALT KHVSP LIGR  
 FVPFAAVAAANCINIPLMRQRELKVGIPVTDENG NRLGESANAAKQAITQVVVSRILMAA  
 PGMAIPPFIMNTLEKKAFLKRFPWMSAPIQVGLVGFCLVFATPLCCALFPQKSSMSVTSL  
 EAELQAKIQESHPELRRVYFNKGL

SEQID No:267

MSQWYELQQLD SKFLEQVHQLYDDSFPM EIRQYLAQWLEKQDWEHAANDVSFATIRF  
 HDLLSQLDDQYSRFSLENNFLLQHNIRKSKRN LQDNFQEDPIQMSMIIYSCLKEERKILE  
 NAQRFNQAQSGNIQSTVMLDKQKELDSKVRNVKDKVMCIEHEIKSLEDLQDEYDFKCK  
 TLQNREHETNGVAKSDQKQEQLLLKKMYLMLDNKRKEVVHKIIELLNVTELTQNALINDE  
 LVEWKRRQQSACIGGPPNACL DQLQNWFTIVAESLQQVRQQLKLEELEQKYTYEHDP  
 ITKNKQVLWDRTFSLFQQLIQSSFVVERQPCMPHPQRPLVLKTGVQFTVKLRLLVKLQ  
 ELNYNLKVKVLFDKDVNERNTVKGFRKFNILGTHTKVMNMEESTNGSLAAEFRHLQLKE  
 QKNAGTRTNEGPLIVTEELHSLSFETQLCQPGLVIDLETTSLPVVISNVSQLPSGWASIL  
 WYNMLVAEPRNLSFFLTTPPCARWAQLSEVLSWQFSSVTKRGLNVDQLNMLGEKLLGP  
 NASPDGLIPWTRFCKENINDKNFPFWLWIESILELIKHLPLWNDGCIMGFISKERERAL  
 LKDQQPGTFLLRFSSESSREGAITFTWVERSQNGGEPDFHAVEPYTKKELSAVTFPDIIR  
 NYKVMAAENIPENPLKYLYPNIDKDHAFGKYYSRPKEAPEPEMELDGPKGTGYIKTELISV  
 SEVHPSRLQTTDNLLPMSPEEFDEVSRIVGSVEFDSMMNTV

SEQID No:268

MEAVLNELVSVEDLLKFEKKFQSEKAAGSVSKSTQFEYAWCLVRTRYND DIRKGIVLLE

ELLPKGSKEEQRDYVFYLA VGN YRLKEYEKALKYVRGLLQTEPQNNQAKELERLIDKAM  
KKDGLVGMAIVGGMALGVAGLAGLIGLAVSKSKS

SEQID No:269

MGAVARAHGGLRVARARES VAGGRHRGAGRPGARAAGAAAGLVRAEAGGRRAGRG  
RRPGRGLPTGGGGGLAAA VGREVAQGLCDAIRLDGGDL LLLRLLQAPELETRVQAARL  
LEQILVAENRDRVARIGLGVILNLAKEREPVELARSVAGILEHMFKHSEETCQRLVAAGG  
LDAVLYWCRRTDPALLRHCALALGNCALHGGQAVQRRMVEKRAAEWLFPLAFSKEDE  
LLRLHACLAVAVLATNKEVEREVERSGTLALVEPLVASLDPGRFARCLVDASDTSQGRG  
PDDLQRLVPLLD SNRLEAQCIGAFYLCAEAAIKSLQGKTKVFSDIGAIQSLKRLVSYSTNG  
TKSALAKRALRLLGEEVPRPILPSVPSWKEAEVQTWLQQIGFSKYCESFREQQVDGDL  
LRLTEELQTDLGMKSGITRKRFFRELTELKTFANYSTCDRSNLADWLGS LDPRFRQYT  
YGLVSCGLDRSLLHRVSEQQLLED CGIHLGVHRARILTAAREMLHSPLPCTGGKPSGDT  
PDVFISYRRNSGSQLASLLKVHLQLHGFSVFIDVEKLEAGKFEDKLIQSVMGARNFVLVL  
SPGALDKCMQDHDCKDWVHKEIVTALSCGKNIVPIIDGFEWPEPQVLPEDMQAVLTFN  
GIKWSHEYQEATIEKIIRFLQGRSSRDSSAGSDTSLEGAAPMGPT

SEQID No:270

MVGEEKMSLRNRLSKSRENPEEDEDQRNPAKESLETPSNGRIDIKQLIAKKIKLTAEAE  
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KIFIARRSLLDELLEVDHIRT IYHMFIAL LILFILSTLVVDYIDEGRLVLEFSLLSYAFGKFPTV  
VWTWWIMFLSTFSVPYFLFQHWATGYSKSSHPLIRSLFHGFLFMIFQIGVLGFGPTYVVL  
AYTLPPASRFIIIFEQIRFVMKAHSFVRENVPRVLNSAKEKSSTVPIPTVNQYLYFLFAPT LI  
YRDSYPRNPTVRWGYVAMKFAQVFGCFYVYIFERLCAPLFRNIKQEPFSARVLVLCV  
FNSILPGVLILFLTFFAFLHCWLN AFAEMLRFGDRMFYKDWWNSTSYSNYYRTWNVVV  
HDWLYYYAYKDFLWFFSKRFKSAAMLAVFAVSAVVHEYALAVCLSFFYPVLFVLFMF FG  
MAFNFIVNDSRKKPIWNVLMWTS LFLGNGVLLCFYSQEWYARRHCPLKNPTFLDYVRP  
RSWTCRYVF

SEQID No:271

MKAMDVLPIKKEKVAYLSGGRDKRGGPILTFPARSNHDIRQEDLRRLISYLACIPSEEV  
CKRGFTVIVDMRGSKWDSIKPLLKILQESFPCCIHALIIPDNFWQKQRTNFGSSKF EF  
ETNMVSLEGLTKVVDPSQLTPEFDGCLEYNHEEWIEIRVAFEDYISNATHMLSRLEELQ  
DILAKKELPQDLEGARNMIEEHSQ LKKKVIKAPIEDLDLEGQKLLQRIQSSESFPKKN SSGS

GNADLQNL L PKVSTMLDRLHSTRQH LHQMWHVRK LKLDQCFQLRLFEQDAEKMFDWI  
 THNKGLFLNSYTEIGTSHPHAMELQTQHNHFAMNCMN VYVNINRIMSVANRLVESGHY  
 ASQQIRQIASQLEQEWKAFAAALDERSTLLDMSSIFHQKAEKYMSNVDSWCKACGEVD  
 LPSELQDLEDAIH HHQGIYEHITLAYSEVSQDGKSLLDKLQRPLTPGSSDSL TASANYSK  
 AVHHVLDVIHEVLHHQRHVRTIWQHRKVRLHQRLQLCVFQQEVQQVLDWIENHGEAFL  
 SKHTGVGKSLHRARALQKRHEDFEEVAQNTYTNADK LLEAAEQLAQTGECDPEEIYQA  
 AHQLEDRIQDFVRRVEQRKILLDMSVSFHTHV KELWTWLEELQKELLDDVYAESVEAVQ  
 DLIKRFGQQQQTTLQVTVNVIKEGEDLIQQLRDSAISSNKT PHNSSINH IETVLQQLDEAQ  
 SQMEELFQERKIKLELFLHVRIFERDAIDIISDLESWNDELSQQMNDFDTEDLTIAEQRLQ  
 HHADKALTMNNLTDFVIHQGDLLQYVNEVQASGV ELLCDRDVDMATRVQDLLEFLHE  
 KQQELDLAAEQHRKHLEQCVQLRHLQAEVKQVLGWIRNGESMLNAGLITASSLQEA EQ  
 LQREHEQFQHAIEKTHQSALQVQQKAEAMLQANHYDMDMIRDCAEKVASHWQQLMLK  
 MEDRLKLVNASVAFYKTSEQVCSVLESLEQEYKREEDWCGGADKLGP NSETDHVTPMI  
 SKHLEQKEAFLKACTLARRNADVFLKYLHRNSVNMPGMVTHIKAPEQQVKNILNELFQR  
 ENRVLHYWTMRKRRLDQCQQYVVFERSAKQALEWIHDNGEFYLS THTSTGSSIQHTQ  
 ELLKEHEEFQITAKQTKERVKLLIQLADGFCEKGHAAHAAEIKKCVTAVDKRYRDFSLRME  
 KYRTSLEKALGISSDSNKSSSKSLQLDIIPASIPGSEVKLRDAAHELNEEKRSARRKEFIM  
 AELIQTEKAYVRDLRECMDTYLWEMTSGVEEIPPGIVNKELIIFGNMQEIYEFHNNIFLKE  
 LEKYEQLPEDVGHCFTWADKFQMYVTYCKNKP DSTQLILEHAGSYFDEIQQRHGLAN  
 SISSYLIKPVQRITKYQLLLKELLTCCEEKGGEIKDGL EVMLSVPKRANDAMHLSMLEGF  
 DENIESQGELILQESFQVWDPKTLIRKGRERH LFLFEMSLVFSKEVKDSSGRSKYLYKSK  
 LFTSELGVTEHVEGDPCKFALWVGRTPTSDNKIVLKASSIENKQDWIKHIREVIQERTIHL  
 KGALKEPIHIPKTAPATRQKGRRDGEDLDSQGDGSSQPDTISIASRTS QNTLDSDKLSG  
 GCELTVVIHDFTACNSNELTIRRGQTVEVLERPHDKPDWCLVRTTDRSPAAEGLVPCGS  
 LCIAHSRSSMEMEGIFNHKDSL SVSSNDASPPASVASLQPHMIGAQSSPGPKRPGNTL  
 RKWLTSPVRRLSSGKADGHVKKLAHKHKSREVRKSADAGSQKDSDDSAATPQDETV  
 EERGRNEGLSSGTL SKSSSSGMQSCGEEEGEEGADAVPLPPPMAIQQH SLLQPDSQD  
 DKASSRLLVRPTSSETPSAAELVSAIEELVKSKMALED RPSSLLVDQGDSSSPSFNPSD  
 NSLLSSSSPIDEMEERKSSSLKRRHYVLQELVETERDYVRDLGYVVEGYMALMKEDGV  
 PDDMKGKDKIVFGNIHQIYDWHRDFFLGELEKCLEDPEKLGSLFVKHERRLHMYIAYCQ  
 NPKPSEHIVSEYIDTFFEDLKQRLGHR LQLTDLLIKPVQRIMKYQLLLKDFLKYSKKASLD  
 TSELERAVEVMCIVPRRCNDMMNVGRLQGFDGKIVAQ GKLLLQDTFLVTDQDAGLLPR  
 CRERRIFLFEQIVIFSEPLDKKKGF SMPGFLFKNSIKVSCLCLEENVENDPCKFALT SRTG  
 DVVETFILHSSSPSVRQTWIHEINQILENQRNFLNALTSP IEYQRNHSGGGGGGGSGAA

AGVGAAAAAGPPVAAAATVAAPAAAAAPPARAGAGPPGSPSLSDTTPPCWSPLQPRA  
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 TDQCPAAEGWIPGFVLGHTSAVIVENPDGTLKKSTSWHTALRLRKKSEKKDKDGKREG  
 KLENGYRKSREGLSNKVSVKLLNPNIYDVPPEFVIPLSEVTCETGETVVLRRCRVCGRP  
 KASITWKGPEHNTLNNDGHYSISYSDLGEATLKIVGVTTEDDGIYTCIAVNDMGSSASSA  
 SLRVLGPGMDGIMVTWKDNFDSFYSEVAELGRGRFSVVKKCDQKGTKRAVATKCFVNK  
 KLMKRDQVTHELGILQSLQHPLLVLGLDFTFETPTSILVLEMADQGRLDCVVRWGSLT  
 EGKIRAHLEGEVLEAVRYLHNCRIHLDLKPENILVDESLAKPTIKLADFGDAVQLNTTYI  
 HQLLGNPEFAAPEIILGNPVSLSDTWSVGVLTIVLLSGVSPFLDDSVETCLNICRLDF  
 SFPDDYFKGVSQKAKEFVCFLLQEDPAKRPSAALALQEQWLQAGNGRSTGVLDTSRLT  
 SFIERRKHQNDVRPIRSIKNFLQSRLLPRV

SEQID No:272

MRKGLRATAARCGGLGYLLQMLVLPALALLSASGTGSAAQDDDFHELPETFPSDPP  
 EPLPHFLIEPEEAYIVKNKPNLYCKASPATQIYFKCNSEWVHQKDHIVDERVDETSGLIV  
 REVSIEISRQQVEELFGPEDYWCQCVAWSSAGTTKSRKAYVRIAYLRKTFEQEPLGKEV  
 SLEQEVLLQCRPPEGIPVAEVEWLKNEDIIDPVEDRNFYITIDHNLIQARLSDTANYTCV  
 AKNIVAKRKSTTATVIVYVNGGWSTWTEWSVCNSRCGRGYQKRTRTCTNPAPLNGGA  
 FCEGQSVQKIACTTLCPPVDGRWTPWSKWSTCGTECTHWRRRECTAPAPKNGGKDCD  
 GLVLQSKNCTDGLCMQTAPDSDDVALYVGIVIAVIVCLAISVVVALFVYRKNHRDFESDII  
 DSSALNGGFQPVNIKAARQDLLAVPPDLTSAAAMYRGPVYALHDVSDKIPMTNSPILDP  
 LPNLKIKVYNTSGAVSPQDDLSEFTSKLSPQMTQSLENEALS LKNQSLARQTDPSCTA  
 FGSFNSLGGHLIVPNSGVSLIPAGAIPQGRVYEMYVTVHRKETMRPPMDDSQTLLTPV  
 VSCGPPGALLTRPVVLTMHHCADPNTEDWKILLKNQAAQGWEDVVVVGEENFTTPC  
 YIKLDAEACHILTENLSTYALVGHSTTKAAAKRLKLAIFGPLCCSSLEYSIRVYCLDDTQD  
 ALKEILHLERQTGGQLLEPKALHFKGSTHNLRLSIH DIAHSLWKSLLAKYQEIPFYHV  
 WSGSQRN LHCTFTLERFSLNTVELVCKLCVRQVEGEGQIFQLNCTVSEEPTGIDLPLD  
 PANTITVTGPSAFSIPLRQKLCSSLDAPQTRGHDWRMLAHKLNLDRLNYFATKSSP  
 TGVILDLWEAQNFDPGNLSMLAAVLEEMGRHETVVSLAAEGQY

SEQID No:273

MAV FVLLALVAGVLGNEFSILKSPGSV VFRNGNWPI GERIPDVAALSMGFSVKEDLS  
 WPGLAVGNLFHRPRATVMVMVKG VNK LALPPGSVISYPLENAV PFSLDSVANSIHS LFS  
 EETPVVLQLAPSEERVYMGKANSVFEDLSVTLRQLRNRLFQENSVLSSLPLNSLSRNN

EVDLLFLSELQVLHDISSLLSRHKHLAKDHSPDLYSLELAGLDEIGKRYGEDSEQFRDAS  
 KILVDALQKFADDMYSLYGGNAVVELVTVKSFDTSIRKTRTILEAKRAKNPASPYNLAY  
 KYNFEYSVVFNMVLWIMIALALAVIITSYNIWNMDPGYDSIIYRMTNQKIRMD

SEQID No:274

MTFYLFGIRSFPKLWKSPYLGLGPGHSYVSLFLADRCGIRNQQRLFSLKTMSQPNTKAT  
 NLIAKARYLRKDEGSNKQVYSVPHFFLAGAAKERSQMNSQTEDHALAPVRNTIQLPTQP  
 LNSEEWDKLEKEDLKENTGKTSFESWIISQMAGCHSSIDVAKSLLAWVAAKNNGIVSYDL  
 LVKYLYLCVFHMQTSEVIDVFEIMKARYKTLEPRGYSLIRGLIHSDRWREALLLEDIKK  
 VITPSKKNYNDCIQGALLHQDVNTAWNLYQELLGHDIVPMLETLKAFFDFGKDIKDDNYS  
 NKLLDILSYLRNNQLYPGESFAHSIKTWFESEGQCSGCGKTIESIQLSPEEYECLKGKIMR  
 DVIDGGDQYRKTTTPQELKRFENFIKSRPPFDVVIDGLNVAKMFPKVRRESQLLLNVVSQ  
 AKRNLRLLLVLGRKHMLRRSSQWSRDEMEEVQKQASCFFADDISEDDPFLLYATLHSGN  
 HCRFITRDLMRDHKACLPDAKTQRLFFKWQQGHQLAIVNRFPGSKLTFQRILSYDTVVQ  
 TTGDSWHIPYDEDLVERCSCEVPTKWLCCLHQKT

SEQID No:275

MALALAALAAVEPACGSRYQQQLQNEEESGEPEQAAGDAPPPYSSISAESAAYFDYKDE  
 SGFPKPPSYNVATTLPYDEAERTKAEATIPLVGRDEDFVGRDDFDADQLRIGNDGI  
 FMLTFFMAFLFNWIGFFLSFCLTTSAAGRYGAISGFGLSLIKWILIVRFSTYFPGYFDGQY  
 WLWWVFLVLGFLFLRGFINYAKVRKMPETFNLPRTRVLFIY

SEQID No:276

MDPECAQLLPALCAVLVDPGQPVADDTCLEKLLDWFKTVTEGESSVLLQEHPCLVELL  
 SHVLKVQDLSSGVLSFSLRLAGTFAAQENCQYLQQGELLPGLFGEPPGLGRATWAVP  
 TVRSGWIIQGLRSLAQHPSALRFLADHGAVDTIFSLQGDSSLFVASAASQLLVHVLALSM  
 RGGAEGQPCLPGGDWPACAQKIMDHVEESLCSAATPKVTQALNVLTTFGRQCSPWT  
 EALWVRLSPRVACLLERDPIPAHVSFVDLLLCVARSPVFSSSDGSLWETVARALSCLGP  
 THMGPLALGILKLEHCPQALRTQAFQVLLQPLACVLKATVQAPGPPGLLDGTADDATTV  
 DTLLASKSSCAGLLCRTLAHLEELQPLPQRPSWPQASLLGATVTVLRLCDGSAAPASS  
 VGGHLCGTLAGCVRVQRAALDFLGTLSQGTGPQELVTQALAVLLECLESPGSSPTVLK  
 KAFQATLRWLLSSPKTPGCSDLGPLIPQFLRELPVLQKRLCHPCWEVRDSALEFLTQL  
 SRHWGGQADFRCALLASEVPQLALQLLQDPESYVRASAVTAMGQLSSQGLHAPTSPE  
 HAEARQSLFLELLHILSVDESEGFPRAVMQVFTEWLRDGHADAAQDTEQFVATVLQAA

SRDL DWEVRAQGLELALVFLGQTLGPPRTHCPYAVALPEVAPAQPLTEALRALCHVGL  
 FDFAFCALFDCDRPVAQKSCDLLLFLRDKIASYSSSLREARGSPNTASAEATLPRWRAGE  
 QAQPPGDQEPEAVLAMLRLSLDLEGLRSTLAESSDHVEKSPQSLLQDMLATGGFLQGDE  
 ADCY

SEQID No:277

MVNYAWAGRSQRKLWWRSAVLTCKSVVRPGYRGGLQARRSTLLKTCARARATAPG  
 AMKMWAPWTRFYNSCCLCCHVRTGTILLGVWYLIINAVVLLILLSALADPDQYNFSSSE  
 LGGDFEFMDDANMCIAIAISLLMILICAMATYGAYKQRAAWIIPFFCYQIFDFALNMLVAIT  
 VLIYPNSIQEYIRQLPPNFPYRDDVMSVNPTCLVLIILLFISIILTFKGYLISCVWNCYRYING  
 RNSSDVLVYVTSNDTTVLLPPYDDATVNGAAKEPPPPYVSA

SEQID No:278

MNIFDRKINF DALLKFSHITPSTQQHLKKVYASFALCMFVAAAGAYVH MVTHFIQAGLLS  
 ALGSLILMIWLMATPHSHETEQRRLGLLAGFAFLTGVGLGPALEFCIAVNPSILPTAFMGT  
 AMIFTCFTLSALYARRRSYLFLGGILMSALSLLLLSSLG NVFFGSIWLFQANLYVGLVVMC  
 GFVLFD TQLIIEKA EHGDQDYIWHCIDLFLDFITVFRKLMMILAMNEKD KKKKEKK

SEQID No:279

MASILDEYENSLSRSAVLQPGCPSVGIPHSGYVNAQLEKEVPIFTKQRIDFTP SERITSLV  
 VSSNQLCMSLGKDTLLRIDLGKANEPNHVELGRKDDAKVHKMFLDHTGSHLLIALSSTE  
 VLYVNRNGQKVRPLARWKGQLVESVGWNKALGTESSTGPILVGTAQGHIFEAE LSASE  
 GGLFGPAPDLYFRPLYVLNEEGGPAPVCSLEAERGP DGRSFVIATTRQRLFQFIGRAAE  
 GAEAQGFSGLFAAYTDHPPPFREFPSNLGYSELAFYTPKLRSAPRAFAWMMGDGVLY  
 GALDCGRPDSLLSEERVWEYPEGVGPGASPLAIVLTQFHFLLLADRVEAVCTLTGQV  
 VLRDHFLEKFGPLKHMVKDSSTGQLWAYTERAVFRYHVQREARDVWRTYLD MNRFDL  
 AKEYCRERPDCLDTVLAREADFCFRQRRYLESARCYALTQSYFEEIALKFLEARQEEAL  
 AEFLQRKLASLKPAERTQATLLTTWLT ELYLSRLGALQGDPEALTLYREVRNLTQFHPLP  
 LAPLLSLSFP THVLFTSREREREHLSSVCSLCGLWNPSSSLSEEAFSSSCL

SEQID No:280

MTSATSPIILKWDPKSLEIRTLTVERLLEPLVTQVTTLVNTSNKGPSGKKKGRSKKAHV L  
 AASVEQATQNFLEKGEQIAKESQDLKEELVAAVEDVRKQGETMRIASSEFADDPCSSVK  
 RGTMVRAARALLSAVTRLLILADMADVMRLLSHLKIVEEAEAVKNATNEQDLANRFKEF

GKKMVKLNYVAARRQQELKDPHCRDEMAAARGALKKNATMLYTASQAFLRHPDVAAT  
 RANRDYVFKQVQEAIAGISNAAQATSPTDEAKGHTGIGELAAALNEFDNKIILDPMTFSE  
 ARFRPSLEERLESIIISGAALMADSSCTRDDRERIVAECNAVRQALQDLLSEYMNNTGR  
 KEKGDPLNIAIDKMTKKTRDLRRQLRKAVMDHISDSFLETNPVLLVLIEAAKSGNEKEVK  
 EYAQVFREHANKLVEVANLACSSISNNEEGVKLVRMAATQIDSLCPQVINAALTLAARPQS  
 KVAQDNMDVFKDQWEKQVRVLTEAVDDITSVDDFLSVSENHILEDVNBKCVIALQEGDVD  
 TLDRTAGAIRGRAARVIHIINAEMENYEAGVYTEKVLEATKLLSETVMPRFAEQVEVAIEA  
 LSAVNPQPFEENEFDASRLVYDGVDRDIRKAVLMIRTPEELEDSDFEQEDYDVRRTS  
 VQTEDDQLIAGQSARAIMAQLPQEEKAKIAEQVEIFHQEKSKLDAEVAKWDDSGNDIIVL  
 AKQMCMIMMEMTDFTRGKGPLKNTSDVINAACKIAEAGSRMDKLARAVADQCPDSACK  
 QDLLAYLQRIALYCHQLNICKVKAQVQNLGGELIVSGTGVQSTFTTFYEVDCCVIDGGR  
 ASQLSTHLPTCAEGAPIGSGSSDSSMLDSATSLIQAANKLMNAVVLTVKASYVASTKYQ  
 KVYGTAAVNSPVVSWKMKAPKKPLVKREKPEEFQTRVRRGSQKKHISPVQALSEFKA  
 MDSF

SEQID No:281

MSGDSERAVAPGVVPAPCASKVELRLSCRHLLDRDPLTKSDPSVLLQQAQGGWLQV  
 DRTEVVKSSLHPVFSKVFTVDYYFEGVQKLRFEVYDTHGPSGLTCQDDDFLGGMECTL  
 GQIVAQKKMTRPLLLRFGRNAGKSTITVIAEDISGNNGYVELSFQARKLDDKDLFSKSDP  
 FLELYRVNDDGSEQLVYRTEVVKNNLNPVWEPFKVSLNSLCSCEETRPLKCLVWDYDS  
 RGKHDFIGDFTTTFAEMQKAFEEEEQQAQWDCVNAKYKQKKRNYKNSGVVILADKLHR  
 VHSFLDYIMGGCQIHCTVAIDFTASNGDPRNSCSLHHINPYQPNEYLRALVAVGEVCQD  
 YDSDKRFSALGFGARIPPKYEVSDFAINFNPEDECEGIQGVVEAYQNCLPKVQLYGP  
 TNVAPIISKVARMAAAEESTGEASQYYILLITDGVVTDMSDTREAIVRASHLPMSVIIVGV  
 GNADFTDMQILDGDDGVLRSPRGEPALRDIVQFVPFRELKNASPAALAKCVLAEVPKQV  
 VEYYSHKELPPRSLGAQTGEAAASSAP

SEQID No:282

MAAQCVTKVALNVSCANLLDKDIGSKSDPLCVLFLNTSGQQWYEVERTERIKNCLNPQF  
 SKTFIIDYYFEVVQKLKFGVYDIDNKTIELSDDDFLGECECTLGQIVSSKKLTRPLVMKTG  
 RPAGKGSITISAEIKNRVLVLFEMEARKLDNKDLFGKSDPYLEFHKQTSNGNWLMMVHR  
 TEVVKNNLNPVWRPFKISLNSLCYGDMDKTIKVECYDYDNDGSHDLIGTFQTTMTKLKE  
 ASRSSPVEFECINEKKRQKKKSYKNSGVISVKQCEITVECTFLDYIMGGCQLNFTVGVD  
 TGSNGDPRSPDSLHYISPNGVNEYLTALWSVGLVIQDYDADKMFPAGFGAQPQWQ

VSHEFPMNPNPSNPYCNGIQGIVEAYRSCLPQIKLYGPTNFSPIINHVARFAAAATQQQT  
 ASQYFVLLIITDGVITDLDETRQAIVNASRLPMSIIIVGVGGADFSAMEFLDGDGGSRLSPL  
 GEVAIRDIVQFVPFRQFQNAPEALAQCVLAEIPQQVVG YFNTYKLLPPKNPATKQQKQ

SEQID No:283

MAVSASPVISATSSGAGVPGGLFRAEPLYSTPREPPRLTPNMINSFVNNHSNSAGGG  
 GRGNTNTNECRMVDMHGMKVASFLMDGQELICLPQVFDLFLKHLVGGLHTVYTKLKRL  
 DISPVVCTVEQVRILRGLGAIQPGVNRCKLITRKDFETLFTDCTNARRKRQMTRKQAVN  
 SSRPGRPPKRSGLVLQENARLLTHAVPGLLSPGLITPTGITAAAMAEAMKLQMKMLMAM  
 NTLQGNGSQNGTESEPDDLNSNTGGSESSWDKDKMQSPFAAPGPQHGIHAALAGQ  
 PGIGGAPTLNPLQQNHLLTNRLDLPFMMMPHPLLPSLPPASVAMAMNQMNHLNTIAN  
 MAAAAQIHSPLSRAGTSVIKERIPESPSPAPSLEENHRPGSQTSSHTSSSVSSSPSQMD  
 HHLERMEEVPVQIPIMKSPLDKIQLTPGQALPAGFPGPFIADSLSSVETLLTNIQGLLKV  
 ALDNARIQEKQIQQEKELRLELYREREIRENLERQLAVELQSRTTMQKRLKKEKTKRK  
 LQEALFESKRREQVEQALKQATTSDSGLRMLKDTGIPDIEIENNGTPHDSAAMQGGNY  
 YCLEMAQQLYSA

SEQID No:284

MDDSEVESTASILASVKEQEAQFEKLTRALEEERRHVSAQLERVRVSPQDANPLMANG  
 TLTRRHQNGRFVGDADLERQKFSDLKLNGPQDHSLLYSTIPRMQEPGQIVETYTED  
 PEGAMSVVSVETSDDGTTRRTETT VKKVKT VTTTRTVQPVAMGPDGLPVDASSVSNNY  
 IOTLGRDFRKNNGGPGPYVGQAGTATLPRNFHYPPDGYSRHYEDGYPGGSDNYGSL  
 SRVTRIEERYRPSMEGYRAPSRQDVYGPQPQVRVGGSSVDLHRFHPEPYGLEDDQRS  
 MGYDDL DYGMMSDYGTARRTGTPSDPRRRLRSYEDMIGEEVPSDQYYWAPLAQHER  
 GSLASLDSL RKGGPPPPNWRQPELPEVIAMLGFR L DAVKSNAAYLQHLCYRNDKVKT  
 DVRKLKGIPVLVGLLDHPKKEVHLGACGALKNISFGRDQDNKIAIKNCDGVPALVRLLRK  
 ARDMDLTEVITGTLWNLSSHDSIKMEIVDHALHALTDEVIIPHSGWEREPNEDCKPRHIE  
 WESVLTNTAGCLRNVSSEARREARRKLRECDGLVDALIFIVQAEIGQKDSDSL VENCVC  
 LLRNLSYQVHREIPQAERYQEAAPNVANNTGPHAASCFGAKKGKGKKPIEDPANDTVD  
 FPKRTSPARGYELLFQPEVVRIYISLLKESKTPAILEASAGAIQNLCAGRWTYGRYIRSAL  
 RQEKALSAIADLLTNEHERVVKAASGALRNLAVDARNKELIGKHAIPNLVKNLPGGQQN  
 SSWNFSEDTVISILNTINEVIAENLEAAKKLRETQGIEKLVLINKSGNRSEKEVRAAALVLQ  
 TIWGYKELRKPLEKEGWKKSD FQVNLNNASRSQSSHSYDDSTLPLIDRNQKSDNNYST



PNERGDHNRTLDRSGDLGDMEPLKGTTPLMQDEGQESLEEELDLVLDDDEGGQVSYP  
SMQKI

SEQID No:285

MACPALGLEALQPLQPEPPPEPAFSEAQKWIEQVTGRSFGDKDFRTGLENGILLCELLN  
AIKPGLVKKINRLPTPIAGLDNIILFLRGCKELGLKESQLFDPSDLQDTSNRVTVKSLDYSR  
KLKNVLVTIYWLGAANSCTSYSGTTNLKEFEGLLAQMRKDTDDIESPKRSIRD SGYID  
CWDSESRDSLSPPRHGRDDSFDSLDSFGSRSRQTPSPDVVLRGSSDGRGSDSESDLP  
HRKLPDVKKDDMSARRTSHGEPKSAVPFNQYLPNKSNTAYVPAPLRKKKAEREEYR  
KSWSTATSPLGGERPFRYGPRTPVSDDAESTSMFDMRCEEEAAVQPHSRARQEQLQL  
INNQLREEDDKWQDDLARWKSRRRSVSQDLIKKEEERKKMEKLLAGEDGTSERRKSIK  
TYREIVQEKERRERELHEAYKNARSQEEAEGILQQYIERFTISEAVLERLEMPKILERSHS  
TEPNLSSFLNDPNPMKYLRQQSLPPP KFTATVETTIARASVLDTSMSAGSGSPSKTVTP  
KAVPMLTPKPYSQPKNSQDVLKTFKVDGKVSVNGETVHREEEKERECPTVAPAHSLTK  
SQMFEGVARVHGSPLKQDNGSIEINIKKPN SV PQELAAATTEKTEPNSQEDKNDGGKS  
RKGNIELASSE PQHF TTTVTRCSPTVAFVEFPSSPQLKNDVSEEKDQKKPENEMSGKV  
ELVLSQKVVKPKSPEPEATLTFPFLDKMPEANQLHLPNLNSQVDSPSSEKSPVMTPFKF  
WAWDPEEERRRQEKWQQEQERLLQERYQKEQDKLKEEWEKAQKEVEEEEERRYYEE  
ERKIIEDTVVPFTVSSSSADQLSTSSSMTEGSGTMNKIDLGNCQDEKQDRRWKKSFGG  
DDSDLLLKTRES DRLEEKGS LTEGALAHSGNPVSKGVHEDHQLDTEAGAPHCGTNPQL  
AQDPSQNNQTSNPTHSSSEDVKPKTLPLDKSINH QIESP SERRKKSPREHFQAGPFSPC  
SPTPPGQSPNRSISGKKLCSSCGLPLGKGAAMIIETLNLYFHIQCFCRGICKGQLGDAVS  
GTDVRI RNGLLNCNDCYMR SR SAGQPTTL

SEQID No:286

MAARGRRAEPQGREAPGPAGGGGGGSRWAESGSGTSPESGDEEVSGAGSSPVSGG  
VNLFANDGSFLELFKRKMEEEEQRQRQEPPPGPQRPDQSAAAAGPGDPKRKGPGS  
TLSFVGKRRGGNKLALKTGIVAKKQKTEDEVLT SKGDAWAKYMAEVKKYKAHQCGDD  
DKTRPLVK

SEQID No:287

MAAETQTLNFGPEWLRALSSGGSITSPPLSPALPKYKLADYRYGREEMLALFLKDNKIP  
SDLLDKEFLPILQEEPLPPLALVPFTEEEQRNFSMSVNSAAVLRLTGRGGGGGT VVGAPR  
GRSSSRGRGRGRGECGFYQRSFDEVEGVFGRGGG REMHRSQSWEERGDRRFEKP

GRKDVGRPNFEEGGPTSVGRKHEFIRSESENWRIFREEQNGEDEDGGWRLAGSRRD  
 GERWRPHSPDGPRGAGWREHMERRRRFEFDFRDRDDERGYRRVRSRSGSGSIDDDR  
 SLPEWCLEDAEEEMGTDFDSSGAFLSLKKVQKEPIPEEQEMDFRPVDEGEECSDSEGSH  
 NEEAKEPKDTNKKKEGEKTDRVGVEASEETPQTSSSSARPGTPSDHQSQEASQFERKD  
 EPKTEQTEKAAEEETRMENSLPAKVPSRGDEMADVQQPLSQIPSDTASPLILPPPVPN  
 PSPTLRPVETPVVGAPGMGSVSTEPDDEEGLKHLEQQAEMVAYLQDSALDDERLASK  
 LQEHRAKGVSIPLMHEAMQKWYYKDPQGEIQGPFNNQEMAWEFQAGYFTMSLLVKRA  
 CDESFQPLGDIMKMWGRVPFSPGPAPPPHMGELDQERLTRQQELTALYQMQLHQYQ  
 QFLIQQQYAQVLAQQQKAALSSQQQQQLALLLQQFQTLKMRISDQNIIPSVTRSVSPD  
 TGSIWELQPTASQPTVWEGGSVWDLPLDTTTPGPALEQLQQLEKAKAAKLEQERREAE  
 MRAKREEEERKRQEEELRRQEEILRRQEEERKRREEEELARRKQEEALRRQREQEIA  
 LRRQREEEERQQQEEALRRLEERRRREEERRRKQEELLRKQEEEAAKWAREEEEAQRR  
 LEENRLRMEEEAARLRHEEEERKRKELEVQRQKELMRQRQQQQEALRRLQQQQQQQ  
 QLAQMKLPSSSTWGGQSNTTACQSQATLSLAEIQKLEERERQLREEQRRQQRELMK  
 ALQQQQQQQQQKLSGWNVSKPSGTTKSLLEIQQEEARQMKGQQQQQQQHQQPNR  
 ARNNTHSNLHTSIGNSVWGSINTGPPNQWASDLVSSIWSNADTKNSNMGFWD DAVKE  
 VGPRNSTNKNKKELK

SEQID No:288

MVGKCLKQNLLACLVISSVTVFYLGQHAMECHHRIEERSQPVKLESTRTTVRTGLDLKA  
 NKT FayHKDMPLIFIGGVPRSGTTLMRAMLDAHPDIRCGEETRVIPRILALKQMWSRSSK  
 EKIRLDEAGVTDEVLD SAMQAFLLEIIVKHGEPAPYLCNKDPFALKSLTYLSRLFPNAKFL  
 LMVRDGRASVHSMISRKVTIAGFDLNSYRDCLTKWNRAIETMYNQCMVEVGYKKCMLVH  
 YEQLVLHPERWMRTLLKFLQIPWNH SVLHHEEMIGKAGGVSLSKVERSTDQVIKPVNV  
 GALS KWVGKIPPDVLQDMAVIAPMLAKLGYDPYANPPNYGKPD PKIIENTRRVYKGEFQ  
 LPDFLKEKPQTEQVE

SEQID No:289

MSTFRQEDVEDHYEMGEELGSGQFAIVRKCRQKGTGKEYAAKFIKKRRLSSSRRGVSR  
 EEIEREVNILREIRHPNIITLHDIFENKTDVVLILELVSGGELDFLAEKESL TEDEATQFLK  
 QILDGVHYLH SKRIA HFDLKPENIMLLDKNVPNPRIKLIDFGIAHKIEAGNEFKNIFGTPEF  
 VAPEIVNYEPLGLEADMWSIGVITYILLSGASPFLGETKQETLTNISAVNYDFDEEYFSNT  
 SELAKDFIRRLLVKDPKRRMTIAQSLEHSWIKAIRRRNVRGEDSGRKPERRRLKTTRLKE  
 YTIKSHSSLPPNNSYADFERFSKVLEEAAAAEEGLRELQRSRRLCHEDVEALAAIYEEKE

AWYREESDSLQDLRRLRQELLKTEALKRQAQEEAKGALLGTSGLKRRFSRLENRYEA  
LAKQVASEMRFVQDLVRALEQEKLQGVCEGLR

SEQID No:290

MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWSDPS  
GTKTCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYR  
CLVGEFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPC  
GIDKFRGVFEVCCPLAEESDNVDSADAEEEDSDVWWGGADTDYADGSEDKVVEVAEE  
EEVAEEVEEEEADDDDEDEDGDEVEEEEAEPEYEEATERTTTSIATTTTTTTTESVEEVVRVP  
TTAASTPDAVDKYLETGPDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKN  
LPKADKKAVIQHFQEKVESLEQEAANERQQLVETHMARVEAMLNDRRRLALENYITALQ  
AVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYE  
RMNQSLSLLYNVPAAVEEIQDEVDELLQKEQNYSDDLANMISEPRISYGNDALMPSLT  
ETKTTVELLPVNGEFSLDDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGS  
GLTNIKTEEISEVNLDAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIV  
ITLVMLKKKQYTSIHGVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN

SEQID No:291

MMHALEVLNSQETGPTLPRQNSQLPAQVQNGPSQEELEIQRRQLQEQQRQKELERER  
LERERMERERLERERLERERLERERLEQEQLERERQERERQERLERQERLERQERLE  
RQERLDRERQERQERERLERLERERQERERQEQLEREQLEWERERRISSAAAPASVE  
TPLNSVLGDSSASEPGLQAASQPAETPSQQGIVLGPLAPPPPPPLPPGPAQASVALPPP  
PGPPPPPPPLPSTGPPPPPPPPPLPNQVPPPPPPPPAPPLPASGFFLASMSDNRPLTGL  
AAAIAGAKLRKVS RMEDTSFPGGNAIGVNSASSKTD TGRGNGPLPLGGSGLMEEMSA  
LLARRRRRIAEKGSTIETE QKEDKGEDSEPVTSKASSTSTPEPTRKPWERTNTMNGSKSP  
VISRPKSTPLSQPSANGVQTEGLDYDRLKQDILDEMRELTKLKEELIDAIRQELSKSNT  
A

SEQID No:292

RHTRTHRDTRHTYTHAHTDAHTCTHMRD TQMHTHTICRKKYALTNIQAAMGLSDPAA  
QPLLGNNGSANIKLVKNGENQLRKAAEQGQQDPNKNLSPTAVINITSEKLEGKEPHQDS  
SSCEILPSQPRRTKSFLNYYADLET SARELEQNRGNHHGTAEKKSQPVQGGQASTIINGN  
DLLLQKPNRPQSSPEDGQVATVSSSPETKKDHPKTGAKTDCALHRIQN LAPSDEESSW  
TTLSQDSASPSSPDETDIWSDFSQTD PDLPPGWKRVSDIAGTYWHIPTGTTQWERP

VSIPADLQGSRKGLSSVTPSPTPENЕКQPWSDFAVLNGGKINSDIWKDLHAATVNPDP  
 SLKEFEGATLRYASLKL RNAPHPDDDDSCSINS DPEAKCFAVRSLGWVEMAEEDLAPG  
 KSSVAVNNCIRQLSYCKNDIRDTVGIWGEGKDMYLILENDMLSLVDPMDRSVWHSQPIV  
 SIRVWGVGRDNGRDFAYVARDKDTRILKCHVFRC DTPAKAIATSLHEICSKIMAERKNAK  
 ALACSSLQERANVNLDVPLQVDFPTPKTEL VQKFHVQYLGMLPVDPKPVGMDILNSAIEN  
 LMTSSNKEDWLSVNMNVADATVTVISEKNEEEVLVECRVRFLSFMGVGKDVHTFAFIM  
 DTGNQRFECHVFWCEPNAGNVSEAVQAACMLRYQKCLVARPPSQKVRPPPPPADSV  
 TRRVTTNVKRGVLSLIDTLKQKRPVTEMP

SEQID No:293

MAQVAMSTLPVEDEESSES RMVVTFLMSALESMCKELAKSKAEVACIAVYETDVFVVG  
 TERGRAFVNTRKDFQKDFVKYCVEEEEKAAEMHKMKSTTQANRMSVDAVEIETLRKTV  
 EDYFCFCYGKALGKSTVVPVPYEKMLRDQSAVVVQGLPEGVAFKHPENYDLATLKWIL  
 ENKAGISFIIKRPFLEPKKHVGG RVMVTDADRSILSPGGSCGPIKVKTEPTEDSGISLEMA  
 AVTVKEESED PDYYQYNIQAGPSETDDVDEKQPLSKPLQGSHHSSEGNEGTEMEVPA  
 EDSTQHVPSETSEDPEVEVTIEDDDYSPPSKRPKANELPQPPVPEPANAGKRKVREFN  
 FEKWNARITDLRKQVEELFERKYAQAIKAKGPVTIPYPLFQSHVEDLYVEGLPEGIPFRR  
 PSTYGIPRLERILLAKERIRFVIKKHELLNSTREDLQLDKPASGVKEEWYARITKL RKMVD  
 QLFCKKFAEALGSTEAKAVPYQKFEAHPNDLYVEGLPENIPFRSPSWYGIPRLEKIIQVG  
 NRIKFVIKRPELLTHSTTEVTQPRNTNPVKEDWNVRITKL RKQVEEIFNLKFAQALGLTEA  
 VKVPYPVFESNPEFLYVEGLPEGIPFRSPTWFGIPRLERIVRGSNKIKFVVKKPELVISYL  
 PPGMASKINTKALQSPKRPRSPGSNSKVPEIEVTVEGPNNNNNPQTSAVRTPTQTNGSN  
 VPFKPRGREFSFEAWNAKITDLKQKVENL FNEKCGEALGLKQAVKVPFALFESFPEDFY  
 VEGLPEGVPFRRPSTFGIPRLEKILRNKAKIKFIIKKPEMFETAIKESTSSKSPPRKINSSP  
 NVNTTASGVEDLNIIQVTIPDDDNERLSKVEKARQLREQVNDLFSRKFGEAIGMGFPVKV  
 PYRKITINPGCVVVDGMPPGVVSFKAPSYLEISSMRRILDSAEFIKFTVIRPFPGLVINNQLV  
 DQSESEGPVIQESAEPSQLEVPATEEIKETDGSSQIKQEPDPTW

SEQID No:294

MAFVCLAIGCLYTF LISTTFGCTSSSDTEIKVNPPQDFEIVDPGYLG YLYLQWQPPLSLD  
 HFKECTVEYELKYRNIGSETWKTIIITKNLHYKDGFDLNKGIEAKIHTLLPWQCTNGSEVQ  
 SSWAETTYWISPQGIPETKVQDMDCVYYNWQYLLCSWKPGIGVLLDTNYNLFYWYEG  
 L DHALQCVDYIKADGQNIGCRFPYLEASDYKDFYICVNGSSENKPIRSSYFTFQLQNIVKP  
 LPPVYLTF TRESSCEIKLKW SIPLGPIPARCFDYEIEIREDDTTLVTATVENETYTLKTTNE

TRQLCFVVRSKVNIYCSDDGIWSEWSDKQCWEGEDLSKKTLLRFWLPFGFILILVIFVTG  
 LLLRKPNTYPKMIPEFFCDT

SEQID No:295

MAERESGGLGGGAASPPAASPFLGLHIASPPNFRLTHDISLEEFEDLSEITDECGISL  
 QCKDTLSLRPPRAGLLSAGGGGAGSRLQAEMQLQMDLIDATGDTPGAEDDEEDDEER  
 AARRPGAGPPKAESGQEPASRGQGSQGSQGSQGPSSGDTYRPKRPTTLNLFQVPRS  
 QDTLNNNSLGGKHSWQDRVSRSSSPLKTGEQTPPHEHICLSDELPPQSGPAPTDRGT  
 STDSPCRRSTATQMAPPGGPPAAPPGGRGHSHRDRIHYQADVRLATEEEIYLPVQRP  
 PDAAEPTSAFLPPTESRMSVSSDPDPAAYPSTAGRPHPSISEEEEEGFDCLSPPERAEPP  
 GGGWRGSLGEPPPPPRASLSSDTSALSYDSVKYTLVVDEHAQLELVSLRPCFGDYSDE  
 SDSATVYDNCASVSSPYESAIGEYEEAPRPQPPACLSDESTPDEPDVHFSKKFLNVF  
 MSGRSRSSSAESFGLFSCIINGEEQEQTTHRAIFRFVPRHEDELELEVDDPLLVELQAED  
 YWYEAYNMRTGARGVFPAYYAIEVTKEPEHMAALAKNSDWVDQFRVKFLGSVQVPYH  
 KGNDVLCAMQKIATTRRLTVHFNPPSSCVLEISVRGVKIGVKADDSQEAKGNKCSHFF  
 QLKNI<sup>1</sup>FCGYHPKNNKYFGFITKHPADHRFACHV<sup>2</sup>FVSEDSTKALAESVGRA<sup>3</sup>FQQFYKQF  
 VEYTCPTEDIYLE

SEQID No:296

GSELETAMETLINVFHAHSGKEGDKYKLSKKELKELLQTELSGFLDAQKD<sup>1</sup>VD<sup>2</sup>AVDKVMK  
 ELDENG<sup>3</sup>DGEVDFQEYVVLVAALT<sup>4</sup>VACNNFFWENS

SEQID No:297

MASTTTCTRFTDEYQLFEELGKGAFSVVRRCKIPTGQGYAAKIINTKKLSARDHQKLE  
 REARICRLLKHPNIVRLHDSISEEGFHYLVFDLVTGGELFEDIVAREYYSEADASHCIQQI  
 LESVNHCHLNGIVHRDLKPENLLLASKSKGA<sup>1</sup>AVKLAD<sup>2</sup>FGLAIEVQGDQQAWFGFAGTP  
 GYLSPEVLRKDPYGKPVDMWACGVILYILLVGYP<sup>3</sup>PFWD<sup>4</sup>EDQHR<sup>5</sup>LYQQIKAGAYDFPSP  
 EWDTVTPEAKDLINKMLTINPAKRITASEALKHPWICQRSTVASMMHRQETVDCLKKF<sup>6</sup>N  
 ARRLKGA<sup>7</sup>ILTTMLATRNFSAAKSLLKKPDGVKESTESSNTTIED<sup>8</sup>EDVKARKQEIIKVTEQ  
 LIEAINNGDFEAYTKICDPGLTAFEPEALGNLVEGMDFH<sup>9</sup>RFYFENALSKSNKPIHTIILNPH  
 VHLVGDDAACIAYIRLTQYMDGSGMPKTMQSEETRVWHRRDGKWQNVHFHRSGSPT  
 VPIKPPCIPNGKENFSGGTS<sup>10</sup>SLWQNI

## SEQID No:298

MTATEALLRVLLLLLAFGHSTYGAECFPACNPQNGFCEDDNVCRCQPGWQGGLCDQC  
 VTSPGCLHGLCGEPGQCICTDGWDGELCDRDVRACSSAPCANNGTCVSLDGGGLYECS  
 CAPGYSGKDCQKKDGPCVINGSPCQHGGTCVDDEGRASHASCLCPPGFSGNFCEIVA  
 NSCTPNPCENDGVCTDIGGDFRCRCPAGFIDKTC SRPVTNCASSPCQNGGTCLQHTQ  
 VSYECLCKPEFTGLTCVKKRALSPQQVTRLPSGYGLAYRLTPGVHELVPVQQPEHRILKV  
 SMKELNKKTPLLTEGQAICFTILGVLTSLVVLGTVGIVFLNKCETWVSNLRYNHMLRKKK  
 NLLLQYNSGEDLAVNIIFPEKIDMTTFSKEAGDEEI

## SEQID No:299

MATIPDWKLQLLARRRQEEASVRGREKAERERLSQMPAWKRGLLERRRAKLGLSPGE  
 PSPVLGTVEAGPPDPDESAVLLEAIGPVHQNRFRIRQERQQQQQQQQRSEELLAERKPG  
 PLEARERRRPSPGEMRDQSPKGRESREERLSPRETRERRLGIGGAQELSLRPLEARDW  
 RQSPGEVGDRSSRLSEAWKWRLSPGETPERSRLAESREQSPRRKEVESRLSPGESA  
 YQKLGLTEAHKWRPDSRESQEQLVQLEATEWRLRSGEERQDYSEECGRKEEWPVP  
 GVAPKETAELSETLTREAQGNSSAGVEAAEQRPVEDGERGMKPTEGWKWTLNSGKA  
 REWTPRDIEAQTQKLEPPESAELLES PGVEAGEGEAEKEEAGAQRPLRALQNCCSV  
 PSPLPPEDAGTGGLRQQEEEEAVELQPPPPAPLSPPPPAPTAPQPPGDPLMSRLFYGVK  
 AGPGVGAPRRSGHTFTVNPRRSVPPATPATPTSPATVDAAVPGAGKKRYPTAEELVL  
 GGYLRLSRSLAKGSPERHHKQLKISFSETALETTYQYPSESSVLEELGPEPEVPSAPN  
 PPAAQPDDEEDEEELLLLQPELQGGGLRTKALIVDESCRR

## SEQID No:300

MSEHVEPAAPGPGPNGGGGGPAPARGPRTPNLNPINVRDRLFHALFFKMAVTYS  
 RLFPPAFRRRLFEEFVLLKALFVLFVLAYIHIVFSRSPINCLEHVRDKWPREGILRVEVRHN  
 SSRAPVFLQFCDSGGRGSFPGLAVEPGSNLDEDEEEELTMEMFGNSSIKFELDIEP  
 KVFKPPSSTEALNDSQEFPPETPTKVWPQDEYIVEYSLEYGFLRLSQATRQRLSIPVM  
 VVTLDPTRDQCFGDRFSRLLLDEFLGYDDILMSSVKGLAENEENKGFLRNVVSGEHYRF  
 VSMWMARTSYLAFAIMVIFTLSVSMLLRYSHHQIFVFIVDLLQMLEMNMAIAFPAAPLLT  
 VILALVGMEAIMSEFFNDTTTAFYIILIVWLADQYDAICCHTSTSKRHWLRRFFLYHFAYFA  
 YHYRFNGQYSSLALVTSWLFIQHSMIYFFHHYELPAILQQVRIQEMLLQAPPLGPGTPTA  
 LPDDMNNNSGAPATAPDSAGQPPALGPVFELVSKERGWGSAEGSGGVLVGLQ

SEQID No:301

KEQSELDQDLDDVEEVEEEETGEETKLKARQLTVQMMQNPQILAAALQERLDGLVETPT  
GYIESLPRVVKRRVNALKNLQVKCAQIEAKFYEEVHDLERKYAVLYQPLFDKRFEIINAIY  
EPTEECEWKPDEEDEISEELKEKAKIEDEKKDEEKEDPKGIPFWLTVFKNVDLLSDM  
VQEHDEPILKHLKDIKVKFSDAGQPMSEFVLEFHFEPNEYFTNEVLTKTYRMRSEPDDSD  
PFSFDGPEIMGCTGCQIDWKKGKNVTLTKIKKKQKHKGRTVVRTVTKTVSNDSFFNFFA  
PPEVIPKFSADFDDAEAILAADFEIGHFLRERIIPRSVLYFTGEAIEDDDDDYDEEGEEAD  
EGYQLFEEVKSCSKLFQRWLQ

SEQID No:302

GKQNSKLRPEVMQDLLESTDFTEHEIQEWYKGFLRDCPSGHLSMEEFKKIYGNFFPYG  
DASKFAEHVFRFTDANGDGTIDFREIIALSVTSRGKLEQKLKWAFSMYDLGNGYISKA  
EMLEIVQAIYKMVSSVMKMPPEDESTPEKRTEKIFRQMDTNRDGKLSLEEFIRGAKSDPSI  
VRLQCDPSSAGQF

SEQID No:303

MVEKGPEVSGKRRGRNNAASASAAAASAAASAACASPAATAASGAAASSASAAAAS  
AAAAPNNGQNKSLAAAAPNGNSSNSWEEGSSGSSSDEEHGGGGMRVGPQYQAVV  
PDFDPAKLARRSQERDNLGMLVWSPNQNLSEAKLDEYIAIAKEKHGYNMEQALGMLFW  
HKHNIEKSLADLPNFTPFPDEWTVEDKVLFEQAFSFGKTFHRIQQMLPDKSIASLVKFY  
YSWKKTRTKTSVMDRHARKQKRERESEDELEEANGNNPIDIEVDQNKESKKEVPTE  
TVPQVKKEKHSTQAKNRAKRKPPKGMFLSQEDVEAVSANATAATTVLRQLDMELVSVK  
RQIQNIKQTNSALKEKLDGGIEPYRLPEVIQKCNARWTTEEQLLAVQAIRKYGRDFQAIS  
DVIGNKSVVQVKNFFVNYRRRFNIDEVLQEWEAEHGKEETNGPSNQKPKVSPDNSIKM  
PEEEDEAPVLDVRYASAS

SEQID No:304

MSELEKAMVALIDVFHQYSGREGDKHKLKKSELKELINNELSHFLEEIKEQEVDKVMET  
LDNDGDGECDFQEFMAFVAMVTTACHEFFEHE

SEQID No:305

MDDDIAALVVDNGSGMCKAGFAGDDAPRAVFPSIVGRPRHQGVMVGMGQKDSYVGD  
EAQSKRGILTLKYPIEHGIVTNWDDMEKIWHHTFYNELRVAPEEHPVLLTEAPLNPKANR  
EKMTQIMFETFNTPAMYVAIQAVLSLYASGRTTGIVMDSGDGVTHTVPIYEGYALPHAIL

RLDLAGRDLTDYLMKILTERGYSFTTTAEREIVRDIKEKLCYVALDFEQEMATAASSSSL  
 EKSYPDPDGQVITIGNERFRCPEALFQPSFLGMESCGIHETTFNSIMKCDVDIRKDLNAN  
 TVLSGGTTMYPGIADRMQKEITALAPSTMKIKIIPPERKYSVWIGGSILASLSTFQQMWI  
 SKQEYDESGPSIVHRKCF

SEQID No:306

MRECISIHVGQAGVQIGNACWELCYCLEHGIQPDGQMPSDKTIGGGDDSFNTFFSETGA  
 GKHVPRAVFVDLEPTVIDEVRTGTYRQLFHPEQLITGKEDAANNYARGHYTIGKEIIDLV  
 DRIRKLADQCTGLQGFLVFHSFGGGTGSGFTSLLMERLSVDYDGKKSLEFSIYPAPQVS  
 TAVVEPYNSILTTHTTLEHSDCAFMVDNEAIYDICRRNLDIERPTYTNLNLISQIVSSITA  
 SLRFDGALNVDLTEFQTNLVPYPRIHFPLATYAPVISAEEKAYHEQLSVAEITNACFEPAN  
 QMVKCDPRHKGKYMCCLLYRGDVVPKDVNAAIATIKTKRSIQFVDWCPTGFKVGINYQ  
 PPTVPPGGDLAKVQRAVCMLSNTTAAEAWARLDHKFDLMYAKRAVHWHYVGEEMEE  
 GEFSEAREDMAALEKDYEYEVGVDSVEGEGEEEGEEY

SEQID No:307

MREIVHIQAGQCGNQIGAKFWEVISDEHGIDPTGTYHGDSDLQLDRISVYYNEATGGKY  
 VPRAILVDLEPGTMDSVRSRSGPFGQIFRPDNFVFGQSGAGNNWAKGHYTEGAELVDSVL  
 DVVRKEAESDCCLQGFLTHSLGGGTGSGMGTLISKIREEYPDRIMNTFSVVPSPKVS  
 DTVVEPYNATLSVHQLVENTDETYCIDNEALYDICFRTLKLTPTTYGDLNHLVSATMSGV  
 TTCLRFPGQLNADLRKLAVNMVFPRLHFFMPGFAPLTSRGSQQYRALTVPELTQQVF  
 DAKNMMAACDPRHGRYLTVAAVFRGRMSMKEVDEQMLNVQKNSSYFVEWIPNNVK  
 TAVCDIPPRGLKMAVTFIGNSTAIQELFKRISEQFTAMFRRKAFLHWYTGEGMDEMEFT  
 EAESNMNDLVSEYQQYQDATAEEEEEDFGEEAEEEA

SEQID No:308

MEGSLEREAPAGALAAVLKHSSTLPPESTQVRGYDFNRGVNYRALLEAFGTTGFQATN  
 FGRAVQQVNAMIEKKLEPLSQDEQDQHADLTQSRRPLTSCTIFLGYSNLISSGIRETIRYL  
VQHNMDVDLVTTAGGVEEDLIKCLAPTYLGEFSLRGKELRENGINRIGNLLVPNENYCKF  
 EDWLMPILDQMVMEQNTEGVKWTPSKMIARLGKEINNPESVYYWAQKNHIPVFSPALT  
 DGSLGDMIFFHSYKNPGLVLDIVEDLRLINTQAIFAKCTGMILGGGVVKHHIANANLMRN  
 GADYAVYINTAQEFDGSDSGARPDEAVSWGKIRVDAQPVKVYADASLVFPLLVAETFA  
 QKMDAFMHEKNED



## SEQID No:309

MADPKYADLPGIARNEPDVYETSDLPEDDQAEFDAEELTSTSVEHIIVNPNAAYDKFKDK  
 RVGTKGLDFSDRIGKTKRTGYESGEYEMLGEGLGVKETPQQKYQROLLHEVQELTTEVE  
 KIKTTVKESATEEKLTTPVLLAKQLAALKQQLVASHLEKLLGPDAAINLTDPDGALAKRLLL  
 QLEATKNSKGGSGGKTTGTPPDSSLVTYELHSRPEQDKFSQAQKVAELEKRLTELETA  
 VRCDDQDAQNPLSAGLQGACLMETVELLQAKVSALDLAVLDQVEARLQSVLGKVNEIAK  
 HKASVEDADTQSKVHQLYETIQRWSPIASTLPELVQRLVTIKQLHEQAMQFGQLLTHLD  
 TTQQMIANSCLKDNTLLTQVQTTMRENLATVEGNFASIDERMKKLGK

## SEQID No:310

MRKETPPPLVPPAAREWNLPNAPACMERQLEAARYRSDGALLLGASSLSGRCWAGS  
 LWLFKDPCAAPNEGFCASAGVQTEAGVADLTWVGGERGILVASDSGAVELWELDENETLI  
 VSKFCKYEHDDIVSTVSVLSSGTQAVSGSKDICIKVWDLAQQVVLSSYRAHAAQVTCVA  
 ASPHKDSVFLSCSEDNRILLWDTRCPKPASQIGCSAPGYLPTSLAWHPQQSEVVFVFGD  
 ENGTVSLVDTKSTSCVLSSAVHSQCVTGLVFSPHSVPFLASLSEDCSLAVLDSSLSLSELF  
 RSQAHRDFVRDATWSPLNHSLLTTVGWDHQVVHHVVPTEPLPAPGPASVTE

## SEQID No:311

MSISSDEVNFLVYRYLQESGFSHSAFTFGIESHISQSNINGALVPPAALISIIQKGLQYVEA  
 EVSINEDGTLFDGRPIESLSLIDAVMPDVVQTRQQAYRDKLAQQQAAAAAAAAAAAAASQQ  
 GSAKNGENTANGEENGAHTIANNHTDMMEVDGDVEIPPKNKAVVLRGHESEVFICAWNP  
 VSDLLASGSGDSTARIWNLSNSTSGSTQLVLRHCIREGGQDVPSNKDVTSLDWNSEG  
 TLLATGSYDGFARIWTKDGNLASTLGQHKGPFIKALKWNKKGNFILSAGVDKTTIWDAAHT  
 GEAKQQFPFHSAPALDVDWQSNNTFASCSTDMCIHVCKLGQDRPIKTFQGHTNEVNAI  
 KWDPTGNLLASCSDDMTLKIWSMKQDNCVHDLQAHNKEIYTIKWSPTGPGTNNPNANL  
 MLASASFDSTVRLWDVDRGICHTLTKHQEPVYSVAFSPDGRYLASGSFDKCVHIWNTQ  
 TGALVHSYRGTTGGIFEVCWNAAGDKVGASASDGSVCVLDLRK

## SEQID No:312

MDEKVFTKELDQWIEQLNECKQLSESQVKSLCEKAKEILTKESNVQEVRCPTVTCGDV  
 HGQFHDLMELEFRIGGKSPDTNYLFMGDYVDRGYYSVETVTLLVALKVRYRERITILRGN  
 HESRQITQVYGFYDECLRKYGNANVWKYFTDLFDYLPALTALVDGQIFCLHGGLSPSIDTL  
 DHIRALDRLQEVPHGPMCDLLWSDPDDRGGWGISPRGAGYTFGQDISETFNHANGL

TLVSRAHQLVMEGYNWCHDRNVVTIFSAPNYCYRCGNQAAIMELDDTLKYSFLQFDPA  
PRRGEPHVTRRTPDYFL

SEQID No:313

MDDKAFTKELDQWVEQLNECKQLNENQVRTLCEKAKEILTKESNVQEVRCPVTVC GDV  
HGQFHDLME LFRIGGKSPDTNYLFMGDYVDRGYYSVETVLLVALKVRYPERITILRGN  
HESRQITQVYGFYDECLRKYGNANVWKYFTDLFDYLPLTALVDGQIFCLHGGLSPSIDTL  
DHIRALDRLQEVPHGPMCDLLWSDPDDRGGWGISPRGAGYTFGQDISETFNHANGL  
TLVSRAHQLVMEGYNWCHDRNVVTIFSAPNYCYRCGNQAAIMELDDTLKYSFLQFDPA  
PRRGEPHVTRRTPDYFL

SEQID No:314

AAADGDDSLYPIAVLIDELRNEDVQLRLNSIKKLSIALALGVERTRSELLPFLTDTIYDED  
EVLALAEQLGTFTTLVGGPEYVHCLLPPLSLATVEETVVRDKAVESLRAISHEHSPSD  
LEAHFVPLVKRLAGGDWFTSRTSACGLFSVCYPRVSSAVKAELRQYFRNLCSDDTPMV  
RRAAASKLGEFAKVLELDNVKSEIIPMFSNLASDEQDSVRLlaveACVNIAQLLPQEDLE  
ALVMPTLRQAAEDKSWAVRYMVADKFTELQKAVGPEITKTDLVPAFQNLMKDCEAEVR  
AAASHKVKEFCENLSADCRENVIMSQILPCIKELVSDANQHVK SALASVIMGLSPILGKD  
NTIEHLLPLFLAQLKDECPEVRLNIISNLD CVNEVIGIRQLSQSLLPAIVELAEDAKWRVRL  
AII EYMP LLAGQLGVEFFDEKLNSLCMAWLVDHVYAI REAATS NLKKLVEKFGKEWAHA  
TIIPKVLAMSGDPNYLHRMTTLFCINVLSEVCGQDITTKHMLPTVLRMAGDPVANVRFNV  
AKSLQKIGPILDNSTLQSEVKPILEKLTQDQDQDVVKYFAQEALTVLSLA

SEQID No:315

MAEPRQEF EVMEDHAGTYGLGDRKDQGGYTMHQDQEGD TDAGLKESPLQTPTEDGS  
E EPGSETSDAKSTPTAEDVTAPLVDEGAPGKQAAAQPHTEIPEGTTAEEAGIGDTPSLE  
DEAAGHVTQARMVSKSKDGTGSDDKKAKGADGKTKIATPRGAAPP GQKGQANATRIP  
AKTPPAPKTPPSSGEPPKSGDRSGYSSPGSPGTPGSRSRTPSLPTPTREP KKVAVVR  
TPPKSPSSAKSRLQTAPVMPDLKNVKS KIGSTENLKHQP GGGKVQIINKKLDLSNVQS  
KCGSKDNIKHVPGGGSVQIVYK PVDLSKVTSKCGSLGNIHHKPGGGQVEVKSEK LDFK  
DRVQSKIGSLDNITHVPGGGGNKKIETHKLT FRENAKAKTDHGAEIVYKSPVVSGDTS PR  
HLSNVSSSTGSIDMVDSPQLATLADEV SASLAKQGL

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